

CARBOHYDRATES IN THE DIET OF FINNISH ADULTS

**FOCUS ON INTAKE ASSESSMENT AND ASSOCIATIONS
WITH OTHER DIETARY COMPONENTS AND OBESITY**

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ACADEMIC DISSERTATION

To be presented, with the permission of the Faculty of Medicine of
the University of Helsinki, for public examination in Auditorium XV,
University Main Building, on 15 June 2018, at 12 noon.

Helsinki 2018

Cover photo: Kaisu Jouppi, Photographer: kaisujouppi.com

*Dissertationes Scholae Doctoralis Ad Sanitatem Investigandam Univrsitatis
Helsinkiensis*

ISSN 2342-3161 (print)

ISSN 2342-317X (online)

ISBN 978-951-51-4280-1 (paperback)

ISBN 978-951-51-4281-8 (PDF)

Unigrafia

Helsinki 2018

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ABSTRACT

Carbohydrate-containing foods are not solely an important energy source; they also have inherent properties with an impact on human health. The changing food environment sets challenges on understanding the carbohydrate-health relationships. The recent guidelines of the World Health Organization have stimulated public discourse on the relation between added sugars and obesity raising this topic on the public health agenda. However, apart from research on sugar-sweetened beverages, few studies have addressed individual sugars, or added sugars, derived from the overall diet in relation to obesity in adult populations. Moreover, studies on the association of dietary glycaemic index (GI) and glycaemic load (GL) with obesity outcomes have produced mixed results. Some of the methodological challenges affecting non-uniform results are related to food composition databases (FCDBs). The GI is an example of a food property that is not based on chemical analysis, but rather on the blood glucose raising potential of the food. Therefore GI values are seldom incorporated in traditional FCDBs. Furthermore, the validity of dietary self-report methods, such as the food frequency questionnaire (FFQ), in measuring diverse carbohydrate factors requires further study. In this thesis, the term 'carbohydrate factors' includes chemically distinct carbohydrate fractions (e.g. total carbohydrate, starch, total sugars, fructose, lactose, sucrose, dietary fibre) and dietary GI and GL. 'Added sugars' refer to sugars added to foods during their preparation and processing or used as such.

The main aims of this thesis, comprising four individual studies, were to investigate added sugar intake in relation to other nutrients and foods in the diet, and to elucidate the relationship between carbohydrate factors and obesity. Another aim was to provide methodological insight by examining the validity of the FFQ in measuring carbohydrate factors and the suitability of controlled vocabularies in GI value documentation when adding them to the FCDB.

Four Finnish population-based health examination surveys conducted in 2000-2007 served as the data for this study. A total of 13 800 adults aged 25 years and over participated in health examinations that included measured anthropometrics and thorough questionnaires on background data. Subjects' habitual diet was assessed with an FFQ. Dietary data gathered with food records were used as a reference method in FFQ validation. GI values for foods were based on a previous Finnish epidemiological GI database. The controlled vocabularies of the European Food Information Resource Network (EuroFIR) were used to document the GI values when adding them to the Finnish national FCDB (Fineli). Daily intakes of nutrients, food groups, and dietary GI and GL were calculated using the Fineli database. Intake of added sugars was estimated based on sucrose and fructose derived from food sources other than fruits, berries, vegetables, and 100% fruit juices.

On average, 40% of the dietary sugars (sucrose and fructose) were from natural sources (fruits, berries, vegetables, 100% fruit juice), whereas the remaining 60% were added sugars. Subjects with high added sugar intake were on average younger

than subjects with lower added sugar intakes. Intake of added sugar was inversely associated with dietary fibre intake, reflected in lower fruit, vegetable, and rye intakes. Added sugar intake was associated inversely also with fish intake, but positively with intake of butter and butter mixtures. In the meta-analysis of three population-based studies, 23% of the subjects were classified as obese (body mass index, BMI ≥ 30 kg/m²). The likelihood of being obese was 35% lower in the highest quartile of total carbohydrate intake than in the lowest quartile. The associations between total sucrose intake and dietary GL and obesity were also inverse. Dietary GI and fibre intake were not associated with obesity risk. The statistical analyses were adjusted for sex, age, education, leisure-time physical activity, smoking, and energy intake (added sugar and food intake-related analyses also for BMI).

Energy-adjusted Spearman rank-correlation coefficients between carbohydrate factors as measured with the FFQ and food records ranged from 0.37 (total sugars) to 0.69 (lactose) in women, and from 0.27 (total sugars) to 0.70 (lactose) in men. Based on the two methods, 73% of the subjects were correctly classified into the same or adjacent carbohydrate factor distribution quintiles. Subject's age and lower education were associated with diminished agreement between the methods, especially in women. BMI was not associated with the between-method agreement. The controlled vocabularies of EuroFIR were suitable for the documentation of origin and derivation methods of the GI values.

To summarize, the recommendations for added sugar restriction are supported by the associations found between added sugar intake and other dietary components. These associations should be taken into account in studies investigating the relationship between added sugar intake and health outcomes. In this cross-sectional study, high intakes of total carbohydrate, total sucrose, and high dietary GL were associated with decreased risk of obesity. Prospective cohort studies are needed to assess the temporal relation between carbohydrate factors and obesity. Instead of sucrose only, added sugars should be investigated. The results regarding dietary assessment methodology support the validity of the FFQ in ranking subjects according to carbohydrate intake, which is central in nutritional epidemiological studies. The documentation of GI values with controlled vocabularies provides a foundation for comparison of GI databases in the future.

Keywords: Dietary carbohydrate, glycaemic index, added sugar, sucrose, FFQ, food composition database, EuroFIR, adults, obesity

TIIVISTELMÄ

Hiilihydraattipitoiset elintarvikkeet ovat tärkeä energianlähde ja niiden ominaisuuksilla on vaikutusta terveyteen. Ruokaympäristön muuttuminen haastaa ymmärrystä hiilihydraattien ja terveyden välisistä yhteyksistä. Maailman terveysjärjestö WHO:n lisätyn sokerin saantia rajoittavat suositukset ovat nostaneet lisätyn sokerin ja lihavuuden välisen yhteyden julkiseen keskusteluun ja kansanterveyden agendalle. Sokerilla makeutettujen juomien ohella on kuitenkin vain vähän tutkimuksia, jotka ovat selvittäneet koko ruokavaliosta peräisin olevien sokereiden tai lisätyn sokerin yhteyttä lihavuuteen aikuisväestössä. Epidemiologiset tutkimustulokset ruokavalion glykeemisen indeksin (GI) ja kuorman (GL) yhteydestä lihavuuteen ovat myös olleet ristiriitaisia. Menetelmälliset haasteet (esim. erot koostumustietokannoissa), saattavat selittää ristiriitaisia tuloksia. Elintarvikkeen GI on esimerkki ravintotekijästä, joka ei perustu elintarvikkeen kemialliseen analyysiin, vaan sen aiheuttamaan verensokerivasteeseen. Tästä johtuen GI-arvoja ei usein löydy tavanomaisista elintarvikkeiden koostumustietokannoista. Myös ruoankäytön tutkimusmenetelmien, kuten frekvenssityyppisen ruoankäyttökyselyn (FFQ), hyvydestä (validiteetti) erilaisten hiilihydraattialtisteiden mittaamisessa tarvitaan lisää tutkimusta. Tässä väitöstutkimuksessa tarkastellaan hiilihydraatteja kokonaishiilihydraatin ja -sokereiden, fruktoosin, laktoosin, sakkaroosin, ravintokuidun sekä ruokavalion GI:n ja GL:n valossa. Lisätyllä sokerilla tarkoitetaan sokereita jotka on lisätty elintarvikkeeseen tai ruokaan sen valmistuksen yhteydessä tai nautittu sellaisenaan.

Tämän neljästä osatyöstä koostuvan väitöskirjatutkimuksen tavoitteena oli tutkia lisätyn sokerin yhteyksiä muihin ruokavalion osatekijöihin sekä hiilihydraattien saannin sekä ruokavalion GI:n ja GL:n yhteyttä lihavuuteen. Lisäksi tavoitteena oli tutkia ja kehittää hiilihydraattien mittaamiseen liittyviä menetelmiä. Erityisesti tutkittiin FFQ:n validiteettia hiilihydraattien saannin, ruokavalion GI:n ja GL:n mittaamisessa sekä elintarvikkeiden koostumustietokannassa käytössä olevien kontrolloitujen asiansastojen soveltuvuutta GI arvojen kuvaamisessa.

Tutkimus perustui neljään vuosina 2000-2007 kerättyyn suomalaiseen terveystarkastustutkimukseen, joihin osallistui yhteensä 13 800 yli 25-vuotiaista aikuista eri puolilta maata. Terveystarkastuksissa tutkittaville tehtiin antropometriset mittaukset ja heidän taustatietojaan kysyttiin lomakkeilla ja tavanomaista ruoankäyttöä FFQ:lla. Ruokapäiväkirjoilla kerättyjä ruoankäyttötietoja käytettiin vertailumenetelmänä FFQ:n validoinnissa. Aineistojen elintarvikkeille sovellettiin GI-arvot pohjautuen aiempaan suomalaiseen GI-tietokantaan. GI-arvojen dokumentoinnissa käytettiin kontrolloituja asiansastoja (EuroFIR). Päivittäiset ravintoaineiden ja ruoka-aineiden saannit, sekä ruokavalion GI ja GL laskettiin kansallisen elintarvikkeiden koostumustietokannan (Fineli) avulla. Lisätyn sokerin analyysi perustui sakkaroosiin ja fruktoosiin, jotka ovat peräisin muista elintarvikelähteistä kuin hedelmistä, marjoista, kasviksista ja täysmehuista.

Ruokavalion sisältämästä sokereista (sakkaroosi ja fruktoosi), keskimäärin n. 40 % tuli luontaisista lähteistä (hedelmät, marjat, kasvikset, täysmehut), ja loput 60 % oli lisättyä sokeria. Ruokavaliostaan paljon lisättyä sokeria saavat olivat keskimäärin nuorempia kuin ne, joiden lisätyn sokerin saanti oli vähäisempää. Lisätty sokeri oli yhteydessä pienempään kuidun saantiin ja vähäisempään hedelmien, kasvien ja rukiin käyttöön. Toisaalta lisätty sokeri oli yhteydessä vähäisempään kalan käyttöön sekä suurempaan voihin ja voi-kasviöljyseosten käyttöön. Kolmen väestöaineiston yhteisanalyysissä (n=12 342) 23 % tutkittavista luokiteltiin lihavaksi (painoindeksi, BMI ≥ 30 kg/m²). Lihavuuden riski oli 35 % pienempi hiilihydraatin saannin korkeimmassa neljänneksessä verrattuna matalimpaan neljännekseen. Myös sakkaroosin ja GL:n yhteydet lihavuuteen olivat käänteisiä. Ruokavalion GI ja kuidun saanti eivät olleet yhteydessä lihavuuteen. Tilastollisissa analyyseissä huomioitiin sekoittavina tekijöinä tutkittavien sukupuoli, ikä, koulutus, vapaa-ajan liikunta, tupakointi, ja energiansaanti (lisättyä sokeria ja ruoankäyttöä koskevissa analyyseissä myös BMI).

FFQ:n ja ruokapäiväkirjojen väliset energiavakioidut Spearmanin järjestyskorrelaatiokertoimet asettuivat naisilla välille 0.37 (sokerit)-0.69 (laktoosi) ja miehillä välille 0.27 (sokerit)-0.70 (laktoosi). Menetelmien vertailussa keskimäärin 73 % tutkittavista luokiteltiin samaan tai viereiseen hiilihydraattien saannin viidennekseen. FFQ:n ja ruokapäiväkirjojen välinen yhtenevyys heikentyi iän karttuessa sekä siirryttäessä korkeimmasta koulutusluokasta matalampaan, erityisesti naisilla. BMI ei ollut yhteydessä menetelmien väliseen yhtenevyyteen. Tallennettaessa GI-arvoja Fineliin, EuroFIR:n kontrolloidut asiansastot soveltuivat kuvaamaan GI-arvojen alkuperää ja koostamismenetelmiä.

Yhteenvedon voidaan todeta, että tulokset lisätyn sokerin saannin yhteyksistä muuhun ruoankäyttöön tukevat suositusta lisätyn sokerin saannin rajoittamisesta. Havaitut yhteydet tulee huomioida tutkittaessa lisätyn sokerin ja terveyden välisiä yhteyksiä. Runsas hiilihydraattien ja sakkaroosin saanti sekä suuri GL olivat tässä poikkileikkaustutkimuksessa yhteydessä pienempään lihavuuden riskiin. Hiilihydraattien ja lihavuuden välisten ajallisten yhteyksien varmistamiseksi tarvitaan pitkittäistutkimuksia. Sakkaroosin ohella tulee tutkia lisättyä sokeria. Menetelmälliset tutkimustulokset tukevat FFQ:n käyttökelpoisuutta hiilihydraattien suhteellisen saannin mittarina epidemiologisessa ravitsemustutkimuksessa. Elintarvikkeiden koostumustietokantaan tallennettujen GI-arvojen kuvailu kontrolloiduilla sanastoilla luo pohjaa eri maiden välisten GI-tietokantojen vertailulle tulevaisuudessa.

Avainsanat: Ruokavalion hiilihydraatti, glykeeminen indeksi, lisätty sokeri, sakkaroosi, FFQ, elintarvikkeiden koostumustietokanta, EuroFIR, aikuiset, lihavuus

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LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following publications which are referred to in the text by their roman numerals (I-IV):

- I Kaartinen NE, Similä ME, Pakkala H, Korhonen T, Männistö S and Valsta LM (2010). Glycaemic index values in the Finnish food composition database: an approach to standardised value documentation. *Eur J Clin Nutr* **64 Suppl 3**: 68-72.
- II Kaartinen NE, Tapanainen H, Valsta LM, Similä ME, Reinivuo H, Korhonen T, Harald K, Eriksson JG, Peltonen M and Männistö S (2012). Relative validity of a FFQ in measuring carbohydrate fractions, dietary glycaemic index and load: exploring the effects of subject characteristics. *Br J Nutr* **107**: 1367-1375.
- III Kaartinen NE, Similä ME, Kanerva N, Valsta LM, Harald K and Männistö S (2017). Naturally occurring and added sugar in relation to macronutrient intake and food consumption: results from a population-based study in adults. *J Nutr Sci* **6**: e7.
- IV Kaartinen NE, Knekt P, Kanerva N, Valsta LM, Eriksson JG, Rissanen H, Jääskeläinen T and Männistö S (2016). Dietary carbohydrate quantity and quality in relation to obesity: A pooled analysis of three Finnish population-based studies. *Scand J Publ Health* **44**: 385-393.

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ABBREVIATIONS

AISBL	International non-profit Association under the Belgian Law
AOAC	Association of Official Analytical Chemists
ATBC	Alpha-Tocopherol Beta-Carotene Cancer Prevention Study
AUSNUT	Australian Food Supplement and Nutrient Database
BMI	Body mass index
BMR	Basic metabolic rate
CARDIA	Coronary Artery Risk Development in Young Adults Study
CEN	European Committee for Standardization
CI	Confidence interval
CSFII	US Department of Agriculture's Continuing Survey of Food Intakes by Individuals
DHQ	Dietary history questionnaire
DILGOM	Dietary, Lifestyle, and Genetic determinants of Obesity and the Metabolic syndrome Study
DiOGenes	Diet Obesity and Genes Study
DR	Dietary recall
E%	Percentage of total energy
EFCOSUM	European Food Consumption Survey Method Project
EFSA	European Food Safety Authority
EPIC	European Prospective Investigation into Cancer and Nutrition Study
EuroFIR	European Food Information Resource Network
Eurofoods	European project established to improve quality of nutrient data
FAO	Food and Agriculture Organization of the United Nations
FCDB	Food composition database
FFQ	Food frequency questionnaire
FINDIET	Finnish national dietary survey
Fineli	Finnish national food composition database
FINRISK	Finnish national chronic disease risk factor monitoring survey
FR	Food record
GI	Glycaemic index
GL	Glycaemic load
HBSC	Helsinki Birth Cohort Study
Health 2000	Health 2000 Health Examination Survey
HEI	Healthy Eating Index
HPFS	Health Professionals Follow-up Study
IAUC	Incremental area under the curve
INFOODS	International Network of Food Data Systems
Inter99	Danish population-based randomized intervention study
IRAS	Insulin Resistance Atherosclerosis Study
ISO	International Organization for Standardization

MONICA	Multinational Monitoring of trends and determinants in Cardiovascular disease Project
MRDPP	Many Rivers Diabetes Prevention Project, Australia
MUFA	Monounsaturated fatty acids
NCD	Non-communicable diseases
NDNS	National Diet and Nutrition Survey, UK
NHANES	National Health and Nutrition Examination Survey, USA
NHS	Nurses' Health Study
NMES	Non-milk extrinsic sugars
NORFOODS	Nordic project group for coordination of food composition data
NQplus	Nutrition Questionnaires plus – a longitudinal study on diet and health, the Netherlands
OR	Odds ratio
PUFA	Polyunsaturated fatty acids
SACN	Scientific Advisory Committee on Nutrition, UK
SAFA	Saturated fatty acids
SD	Standard deviation
SEASONS	Seasonal Variation of Blood Cholesterol Levels Study, USA
SSB	Sugar-sweetened beverages
STROBE-nut	Strengthening the Reporting of Observational Studies in Epidemiology – extension to nutritional epidemiology
THL	National Institute for Health and Welfare, Finland
USDA	United States Department of Agriculture
WC	Waist circumference
WHI	Women's Health Initiative Dietary Modification Trial
WHO	World Health Organization
WHR	Waist-to-hip ratio

1 INTRODUCTION

In the modern food environment, the diversity of carbohydrate-containing foods has grown due to the food supply offering a wealth of processed foods, which are often characterized by high added sugar and low fibre contents (i.e. foods with low nutrient density) (Augustin et al. 2015). Concomitantly the corner stone of a healthy diet is based on carbohydrate-rich foods, such as fruits and fibre-rich cereal products, contributing to the intake of central nutrients along with naturally occurring sugars (Nordic Council of Ministers 2014). This apparent duality emphasizes the view that carbohydrate-containing foods are not solely an important energy source, but also have inherent properties with an impact on health (Nishida and Martinez Nocito 2007).

At the nutrient level, carbohydrates are generally divided into chemically distinguishable fractions that either provide energy for metabolism (e.g. sugars and starch) or are indigestible in the human gastrointestinal tract (e.g. dietary fibre) (Cummings and Stephen 2007). In the early 1980s, the glycaemic index (GI) was introduced as a classification system of carbohydrate-containing foods based on their postprandial blood glucose response (Jenkins et al. 1981). The GI concept has subsequently been applied to whole diets to enable epidemiological research investigating the relation between carbohydrate quality and health outcomes (Venn and Green 2007). Beside GI, the glycaemic load (GL), applied at both food level and diet level, was devised to simultaneously take into account carbohydrate quality and quantity (Salmeron et al. 1997, Salmerón et al. 1997, Venn and Green 2007).

Recently, high-sugar and high-GI diets have received negative publicity with regard to chronic non-communicable diseases and their risk factors (Jakobsen et al. 2010, Schwingshackl and Hoffmann 2013, Te Morenga et al. 2014). The strong link between sugar-sweetened beverages (SSBs) and obesity found in both randomized controlled trials and prospective cohort studies has strengthened the public health agenda on restricting added sugar intake (Te Morenga et al. 2013, Malik et al. 2013, WHO 2015, Scientific Advisory Committee on Nutrition 2015). Globally, obesity prevalence has tripled in men, and doubled in women over the past 40 years (WHO 2003, NCD Risk Factor Collaboration 2016). In Finland, obesity prevalence also remains high (Männistö et al. 2015). Finding effective strategies to prevent obesity would have a large impact on public health, and diminish the economic burden associated with chronic diseases (WHO 2003). However, the evidence of the long-term association between dietary carbohydrates or dietary GI and GL and obesity remains inconclusive.

The relationship between carbohydrate intake and obesity seems biologically plausible. All carbohydrate-rich foods elicit various physiological effects involved in energy balance regulation of the human body, thereby potentially affecting obesity risk. It is anticipated that the wide availability and the hedonic value of highly palatable foods (e.g. sugar-containing sweet foods) may override physiological mechanisms of energy balance through sweet-tasting mechanisms in the mouth, gut,

and reward regions in the brain (Ochoa et al. 2015). Moreover, carbohydrate-rich foods that induce a high rise in blood glucose and insulin levels (e.g. high GI foods) are suggested to lead to an imbalance in metabolic fluxes, causing reactive hypoglycaemia, and thus, excessive hunger and overeating (Ludwig 2002). Fibre-rich foods have been found to counteract these phenomena by delaying gastric emptying and glucose absorption (Weickert and Pfeiffer 2008).

Regarding sugars, SSBs are the main carbohydrate-related measure associated with adverse health outcomes, including obesity (Te Morenga et al. 2013, Khan and Sievenpiper 2016). Only a few population-based studies have investigated individual sugars or estimated added sugar intake from overall diet in relation to obesity. The high inter-correlation of nutrients has led some investigators to criticize added sugar recommendations since the recommended levels of both added sugar and fat may prove difficult to achieve in practice (Erickson and Slavin 2015). It has been hypothesized that high added sugar intake is associated with poor diet quality, but associations between added sugar intake and other nutrients and foods in the diet are insufficiently documented in modern adult populations (Louie and Tapsell 2015).

Epidemiological studies investigating the relationship between dietary carbohydrates and obesity outcomes face several methodological challenges that might hamper the possibilities of finding significant associations. Accurate measurement of long-term habitual diet of individuals has proven difficult and requires continuous development of self-report dietary methods and characterization of the associated errors (Subar et al. 2015). Moreover, food composition databases (FCDBs) do not contain all dietary factors of interest. Chemical analysis of foods is regarded as the gold standard of food composition information, but added sugars are not chemically distinguishable from naturally occurring sugars, and no standardized estimation method of added sugars exists (Louie et al. 2015a). In addition, the GI should be measured through quantification of blood glucose response in a group of subjects according to a defined protocol (Brouns et al. 2005, International Organization for Standardization 2010). The lack of measured GI values for most foods predisposes epidemiological studies to subjective decisions in the compilation of large GI datasets (van Bakel et al. 2009b). An important goal is to improve the transparency of food GI-values in databases.

The aim of this thesis was to examine carbohydrate measurement methodology in epidemiological studies from the view-point of food composition databases and the food frequency questionnaire used in dietary assessment of the Finnish adult population. Furthermore, cross-sectional associations of added sugar intake with other components of the diet and the associations between carbohydrate intake, dietary GI and GL, and obesity were investigated.

2 REVIEW OF THE LITERATURE

2.1 DEFINITIONS OF DIETARY CARBOHYDRATES

Carbohydrates continue to be the main energy source in human diets, with cereal products, fruits, vegetables, and milk products representing the major food sources (WHO 1998). The nutritional characterization of dietary carbohydrates comprises several approaches (Englyst et al. 2007). These are outlined in the following sections. The different approaches together have formed the basis and theory for epidemiological research investigating the relationship between dietary carbohydrates and health outcomes.

2.1.1 CHEMICAL CHARACTERIZATION

Primarily, carbohydrates are classified according to their chemistry (Cummings and Stephen 2007, Nordic Council of Ministers 2014). A carbohydrate molecule consists of carbon, hydrogen, and oxygen. Based on the degree of molecule polymerization, carbohydrates are divided into three principal groups: sugars, oligosaccharides, and polysaccharides.

Sugars include monosaccharides (e.g. glucose, galactose, fructose; molecules with one monomeric unit), disaccharides (e.g. sucrose, lactose, maltose; molecules with two monomeric units), and polyols (e.g. sorbitol, mannitol; the sugar alcohols). The oligosaccharides include malto-oligosaccharides (e.g. maltodextrins), and other oligosaccharides (e.g. inulin, fructo-oligosaccharides). Polysaccharides are divided into non-starch polysaccharides (e.g. cellulose, hemicellulose, pectin) and starch. The latter consists solely of glucose molecules, which can be in either non-branched (amylose) or branched chemical configuration (amylopectin).

The chemical analysis techniques of carbohydrates in food have evolved in the past 50 years and include liquid chromatographic techniques, coupled with mass spectrometry or enzyme-linked colorimetric assays (Eliasson 2017, Englyst et al. 2007).

2.1.2 PHYSIOLOGY-BASED CHARACTERIZATION

Glycaemic carbohydrate and dietary fibre

A central physiological function of carbohydrates is to raise blood glucose concentration, thereby providing energy for body processes. After food ingestion, carbohydrates are first handled in the upper part of the gastrointestinal tract through enzyme-driven digestion, followed by absorption as sugar molecules. These are further metabolized in the body. In the literature, carbohydrate providing glucose for metabolism is referred to as glycaemic carbohydrate (Cummings and Stephen 2007).

In the lower part of the gastrointestinal tract, carbohydrates resistant to digestion are exposed to microbiota-driven fermentation (resistant carbohydrates) (Cummings

and Stephen 2007, Elia and Cummings 2007). In addition, resistant carbohydrates contribute to an increase in faecal weight and accelerate intestinal transit time, representing functional health effects (Elia and Cummings 2007, Stephen et al. 2017). The resistant carbohydrates essentially include the non-starch polysaccharides (both water-soluble and water-insoluble).

Dietary fibre is used to characterize indigestible carbohydrates and associated substances (Cummings and Stephen 2007, Nordic Council of Ministers 2014). The original conception of dietary fibre is “the proportion of food which is derived from the cellular walls of plants which is digested very poorly in human beings” (Trowell 1972). From the chemical perspective, dietary fibre may, in addition to non-starch polysaccharides, include resistant oligosaccharides, resistant starch, lignin, and other minor components, depending on chemical assessment method (Englyst et al. 2007). The above mentioned substances are included in the fibre definition of the European Commission legislation on food labelling (European Commission 2008), which is followed in the Nordic countries, including Finland (Nordic Council of Ministers 2014). Heterogeneity of the chemical assessment methods has provoked debate on the exact definition of dietary fibre (Englyst et al. 2007). Currently, the most common methods to assess dietary fibres are the Association of Official Analytical Chemists International (AOAC) methods (Stephen et al. 2017). Despite heterogeneous definitions, the term has proven beneficial in understanding health effects of dietary carbohydrates (Englyst et al. 2007).

Glycaemic index and load

Another way to classify dietary carbohydrates based on physiology, the glycaemic index (GI), was proposed in the early 1980s (Jenkins et al. 1981). This term is used to classify carbohydrate containing foods based on their potential to raise postprandial blood glucose concentrations, i.e. one property of the carbohydrate quality of food. The GI is defined as the incremental area under the blood glucose response curve (IAUC) elicited by a food portion containing 50 g of available carbohydrate, and expressed as a percentage of the blood glucose response elicited by 50 g of available carbohydrate from a reference food (glucose solution or white bread), and consumed by the same subject (WHO 1998).

Based on a Joint FAO/WHO Expert consultation and results from interlaboratory studies, the measurement methodology of food GI is specified by an ISO standard (WHO 1998, Wolever et al. 2003, Wolever et al. 2008, International Organization for Standardization 2010). In short, a test series is organized during which subjects are provided with the test food and the reference food on separate days. During testing, the subject consumes the food or beverage, and the change in blood glucose concentration is measured. By definition, the IAUC calculation is started simultaneously with eating and continued for two hours. The GI value of the food is first calculated for each subject, and thereafter, the mean of all obtained GI values is calculated to obtain the GI value of the food tested. This is done to control for the naturally wide variety of glucose responses between individuals.

By definition, the GI is independent of food carbohydrate content (WHO 1998). The term glycaemic load (GL) was introduced to take into account the effect of

carbohydrate portion size (quantity) on postprandial glucose responses (Salmeron et al. 1997, Salmerón et al. 1997). The GL value of a food is calculated by multiplying the food GI with the gram amount of available carbohydrate of the food portion and dividing by 100.

GI (and thereby GL) is a measure relating to the particular food itself. Thus, the food GI (and thereby GL) is influenced by several factors. These include the monosaccharide profile and absorption, the nature of the starch component, food origin (e.g. plant variety), ripeness in case of fresh foods, food storage, and food processing (Liljeberg et al. 1992, Järvi et al. 1995, Soh and Brand-Miller 1999, Östman et al. 2001, Leeman et al. 2005).

Dietary glycaemic index and load

The epidemiological interest in dietary carbohydrates and the role of GI and GL as chronic disease risk factors produced the need to apply food GI and GL to entire diets. For this purpose, the dietary GI and GL values were introduced (Venn and Green 2007). Dietary GI is calculated from GI values of the foods in the diet by proportioning them according to the contribution of the corresponding carbohydrate foods in the diet. To obtain the dietary GL value, the dietary GI is multiplied with the carbohydrate content of the diet and divided by 100.

In general, dietary GI is interpreted as a measure of the overall carbohydrate quality in the diet. In contrast, dietary GL represents an indicator of the glucose response by the total amount of carbohydrate consumed within a diet (Venn and Green 2007).

Carbohydrate-related terminology

In this thesis, the term carbohydrate factors is used to cover chemically and physiologically characterized carbohydrate fractions (e.g. total glycaemic carbohydrate, starch, total sugars, lactose, sucrose, fructose, dietary fibre), as well as dietary GI and GL.

2.1.3 FOOD SOURCE-BASED CHARACTERIZATION OF SUGARS

In food preparation and processing sugars are added to foods to improve their shelf life (preservative), structure, and appearance as well as to increase food palatability. Other dietary sources of sugars include intact fruits and vegetables, which are used as such or in food preparation in households and by the food industry. The food source needs to be taken into account when considering the nutritional value and overall health effect of sugars.

The United Kingdom Department of Health Committee introduced the term intrinsic sugars to describe those sugars retained in intact cellular structures of e.g. fruits and vegetables (Great Britain Department of Health 1989). As their counterpart, the term extrinsic sugars were introduced. Since lactose (extrinsic sugar) is mainly derived from milk, which was considered to have nutritional benefits, non-milk extrinsic sugars (NMES) were distinctly defined (=extrinsic sugars excluding lactose). In addition, 50% of sugars in processed and cooked fruits and vegetables

were assigned to the extrinsic sugar category in the NMES definition. It was considered that extrinsic sugars should be restricted in the diet.

In the year 1978, Southgate and colleagues (Southgate et al. 1978) defined the term free sugar as all mono and disaccharides present in a food, including lactose. The term was primarily used by food analysts to distinguish hydrolysed components detected by chromatography and colorimetric methods. However, in recent years, the term free sugar has adopted a meaning similar to NMES (Cummings and Stephen 2007). WHO has used the term free sugar in its reports and recommendations, defining it as all monosaccharides and disaccharides added to foods by the manufacturer, cook, or consumer, plus sugars naturally present in honey, syrups, and fruit juices (WHO 2003). In the more recent guidelines fruit juice concentrates are also included in the definition of free sugar (WHO 2015). The Scientific Advisory Committee on Nutrition in United Kingdom has recently adopted the term free sugar to replace the term NMES (Scientific Advisory Committee on Nutrition 2015).

The term added sugars used in the United States comprises sugars added to foods during food processing and preparation. The term is, in essence, very similar to free sugars, although pure fruit juices and pureed fruits and vegetables are not included in this definition (Institute of Medicine 2001, US Food and Drug Administration 2016). In the Nordic countries, added sugars refer to refined sugars including sucrose, fructose, glucose, starch hydrolysates and other isolated sugar preparations that are used as such or added during food preparation and manufacturing (Nordic Council of Ministers 2014).

2.2 ASSESSMENT OF DIETARY CARBOHYDRATES

2.2.1 DIETARY INTAKE ASSESSMENT METHODS

The main methods applied in intake assessment of individuals comprise food frequency questionnaires (FFQ), food records (FR), and 24-hour dietary recalls (24-hour DR) (Patterson and Pietinen 2004). All of these methods are based on subject self-report. In addition, certain aspects of the diet can be assessed with biomarkers analysed from biological samples. The general features as well as the advantages and limitations related to the main dietary methods are summarized in Table 1.

Overall, dietary self-report methods are inherently prone to measurement error originating inter alia from the inability of subjects to fully and accurately recall their food consumption (Patterson and Pietinen 2004, Subar et al. 2015). Biomarkers represent a more objective measurement, but require validation to prove reliable in reflecting long-term intake in free-living populations (Corella and Ordovas 2015). In the case of dietary carbohydrates, several potential biomarkers have been identified and are under continuous investigation with regard to their suitability in epidemiological research settings (Hedrick et al. 2012, Naska et al. 2017). These include 24-hour urinary sucrose (Tasevska 2015), corn- and sugar cane-derived carbon stable isotope biomarkers of sugar intake (Jahren et al. 2014), and plasma

alkylresorcinols as markers of whole grain and rye intake (Landberg et al. 2008, Söderholm et al. 2009). The combination of the different dietary methods with appropriate statistical modelling to quantify and correct for measurement error represents one area of progress in nutritional epidemiological research (Bennett et al. 2017).

In practice, the choice of the main method in an epidemiological study is dependent on the study aim and the research resources available (Patterson and Pietinen 2004). A balance between perceived accuracy and overall feasibility should be achieved. Epidemiological studies generally focus on habitual food intake over a long time period when investigating the association between diet and health outcomes (Willett and Lenart 2013). Conceptually, subject ranking according to intake (i.e. discrimination between individuals) is the main objective of epidemiological diet assessment, and FFQs have until recently been the prevailing epidemiological dietary assessment tool (Willett 2013, Subar et al. 2015). Despite some inherent errors, FFQ-based findings have contributed to the evidence base behind public health policy and nutrition recommendations (Satija et al. 2015).

Regarding carbohydrate intake assessment, individuals consume carbohydrates virtually daily, as they are derived from several food sources. Given this assumption, it is critical that the FFQ items incorporate all carbohydrate sources relevant for the given study population. The construction of an informative FFQ requires expertise (Willett 2013). Dietary assessment with FR or 24-hour DR within a given study population can be utilized in the construction of comprehensive FFQs. Depending on the overall research setting and study purpose, FFQs may pursue assessment of a specific dietary factor or have a comprehensive (overall diet) design (Cade et al. 2004). Portion sizes can be absent (qualitative FFQ), predefined and fixed (semi-quantitative FFQ), or ascertained directly as a part of the questionnaire (quantitative FFQ). The clear advantage of whole-diet FFQs for epidemiological studies is that they allow for estimation of total energy intake, which can be used in adjustment when investigating diet-health relationships. Dietary data gathered by short-term methods, which are perceived as more accurate, are often used in FFQ validation studies as reference methods (see Section 2.2.3).

Table 1. Overview of dietary intake assessment methods and their advantages and limitations.

	Food frequency questionnaire	Food record /diary	24-hour dietary recall	Biomarkers
Aim of measurement	<ul style="list-style-type: none">Habitual long-term dietSubject ranking	<ul style="list-style-type: none">Current short-term dietAbsolute intakes	<ul style="list-style-type: none">Current short-term diet (may include repeated measures to model usual long-term intakes)Absolute intakes	<ul style="list-style-type: none">Intake of a specific nutrientAbsolute intake (recovery)Correlation with intake (concentration)
Setting	<ul style="list-style-type: none">Retrospective	<ul style="list-style-type: none">Prospective	<ul style="list-style-type: none">Retrospective	<ul style="list-style-type: none">Retrospective
Typical time frame	<ul style="list-style-type: none">Previous 6-12 months	<ul style="list-style-type: none">3-7 consecutive days	<ul style="list-style-type: none">Previous day	<ul style="list-style-type: none">Previous hours to several months depending on biomarker
Practical application	<ul style="list-style-type: none">Subjects report their usual consumption frequency for a predefined food list during defined time period.	<ul style="list-style-type: none">Subjects detail everything they eat and drink during the predefined period.	<ul style="list-style-type: none">Subjects are interviewed about their diet during the previous day/past 24-hours.	<ul style="list-style-type: none">Biological samples (e.g. urine, blood) are collected and analysed following detailed protocols.
Portion size estimation	<ul style="list-style-type: none">Portion sizes: absent, fixed (predefined) or open	<ul style="list-style-type: none">Picture books, household measures, standard portions, scales	<ul style="list-style-type: none">Picture books, household measures, standard portions, dish models	
Advantages	<ul style="list-style-type: none">Feasible in large studies (inexpensive)Low burden for subjectsCan be self-administered	<ul style="list-style-type: none">Feasibility in large studies depends on resourcesDoes not rely on memory (recording on meal-by-meal basis)Provide data for FFQ validation	<ul style="list-style-type: none">Feasibility in large studies depends on resourcesDoes not affect subject's eating habits (unannounced)Does not require literacyProvide data for FFQ validation	<ul style="list-style-type: none">Independent of subject's memory/skillsProvide data for validation of dietary self-report methodsCan improve accuracy of dietary self-report (prediction scores)
Limitations	<ul style="list-style-type: none">Relies on memory and cognitive estimation skillsLack of detailMisreporting due to social desirability and memory items require updates (time- and population-specificity)	<ul style="list-style-type: none">Requires literacy skills and high subject motivationMisreporting due to social desirability and fatigueProcess tends to modify eating habits	<ul style="list-style-type: none">Relies on memory and perception of portion sizesRequires trained and qualified interviewersMisreporting due to social desirability and memory	<ul style="list-style-type: none">Feasible only in subpopulations of large studiesLack of available biomarkersSensitivity to intake, time integration, sample collection, processing, storage, and analysis

Contents adapted from Willett W. Nutritional Epidemiology, 3rd ed, New York: Oxford University Press, 2013 and Patterson and Pietinen 2004.

2.2.2 ROLE OF FOOD COMPOSITION DATABASES

Principles and history

Food composition databases (FCDBs) form the foundation of nutrition research as they are used to convert food consumption data to nutrient intakes. In addition to nutritional researchers, FCDBs are utilized by the food industry, public health nutritionists, consumers, and policy makers (Finglas et al. 2014).

The history of FCDBs dates back to the late 19th century, when the first tables were published in Europe (Koenig 1878) and the United States (Atwater 1896). Thereafter, work related to food composition has evolved on the basis of national requirements within countries. Over the past 30 years, several international co-operative actions have pursued compatibility of food composition information across countries. These actions include the International Network of Food Data Systems (INFOODS, established in 1984) with regional networks in Europe (Eurofoods, established in 1982) and the Nordic countries (NORFOODS, established in 1982) (Murphy et al. 2016). Further European milestones were set within European Union funded projects, including Cost Action 99 (years 1995-1999), European Food Consumption Survey Method project (EFCOSUM years 1999-2001), and European Food Information Resource (EuroFIR) Network of Excellence (years 2005-2010), its continuation projects EuroFIR Nexus (years 2011-2013) and its continuum association EuroFIR AISBL (Westenbrink et al. 2016). Common for the actions was the aim to establish guidelines for production, management, and use of FCDBs, develop sustainable nutritional calculation procedures, establish compatible food classification and description principles, and improve nutritional data availability for users (Ireland et al. 2002, Slimani et al. 2007b, Reinivuo et al. 2009, Ireland and Møller 2010).

Management of FCDBs

The continuously changing product formulations of the industry make the update of comprehensive (e.g. national) FCDBs demanding. At the same time, the quality of the FCDB is among the fundamental elements of reliable nutritional epidemiological research (Slimani et al. 2007b). Essential features of FCDBs include the accuracy of the dietary factor values, uniformity of the food analysis methods concerning the given dietary factor, specificity when food processing is known to affect the given dietary factor, and completeness of the dataset (Slimani et al. 2007b, Willett and Sampson 2013). In practice, this kind of immense information requires specified data structures and quality schemes in order to be manageable and traceable (Finglas et al. 2014).

The EuroFIR project initiated a process of developing a food composition data standard to facilitate management and interchange of food composition data within Europe (Becker et al. 2008, Becker and CEN/TC387 Food Data 2010, Finglas et al. 2014). The standard was approved by the European Committee for Standardization in November 2012 and became a national standard in Finland in 2013 (Finnish Standards Association 2013). This standard informs the use of controlled vocabularies, of which the EuroFIR thesauri are examples (Møller et al. 2008).

These thesauri are used to explicitly describe any component (e.g. nutrient or other dietary factor) of the FCDB. The expansion of FCDBs with new dietary factors calls for their explicit documentation as part of the FCDB framework. In this thesis, the suitability of the EuroFIR thesauri for describing glycaemic index (GI) values is considered.

Carbohydrate factors in food composition databases

The FCDBs used in different countries may not be directly comparable due to varying definitions, modes of expression, and completeness of a given dietary factor (Deharveng et al. 1999, Hörnell et al. 2017). Among others, the European Prospective Investigation into Cancer and Nutrition (EPIC) nutrient database project has demonstrated challenges of standardizing nutrient databases across 10 European countries (Slimani et al. 2007a). For example, for total carbohydrate the mode of expression as well as the derivation method and whether dietary fibre is included or not differed between the European countries. While, total sugars and starch were graded as comparable, the comparability of dietary fibre was found to be food group dependent (Slimani et al. 2007a). Regarding epidemiological research on carbohydrates, the authors concluded that harmonization attempts would especially benefit factors with a greater level of incompleteness (e.g. sugars and starch) or specific standardization difficulties (e.g. dietary fibre). Whenever replenishments are needed, a clear documentation of the new dietary factors is essential. For example, recent studies concerning population-based intake estimates of fructose in the United States (Vos et al. 2008) and the Netherlands (Sluik et al. 2015) include a general description for derivation of fructose values.

Overall, the origin and derivation methods for carbohydrate values or other components of FCDBs are rarely clearly referenced in epidemiological study reports. Transparency of FCDB-related issues in reporting has been recently recommended in the STROBE Statement for Observational Studies in Nutritional Epidemiology (STROBE-nut) (Hörnell et al. 2017).

GI in food composition databases

In the past 20 years, epidemiological research on health effects of dietary GI has increased substantially (Venn and Green 2007, Augustin et al. 2015). Since GI values are not standard components of FCDBs, researchers are directed towards compiling GI values for large amounts of food items included in the datasets. The earliest descriptions of GI databases for epidemiological research were published in 2006 (Flood et al. 2006, Neuhouwer et al. 2006, Olendzki et al. 2006), and thereafter, at a steady pace (Table 2). It is noteworthy that there is large variation in the size of the GI databases. Common for all the GI data set descriptions is profiting from regularly amended and extended international tables of GI values as the main information source (Foster-Powell and Miller 1995, Foster-Powell et al. 2002, Atkinson et al. 2008). However, these tables have mainly included Australian and American foods that are not necessarily comparable with foods consumed in other countries. This concern has been uniformly raised among European researchers (van Bakel et al. 2009b). Knowledge on local and culture-specific food preparation

methods is important with regard to GI values since these are affected not only by ingredients and carbohydrate content but also by cooking method, food processing, and plant variety (Järvi et al. 1995, Leeman et al. 2005, Henry et al. 2005).

The process of compiling GI datasets has been recognized to rely on subjective decisions. Overall, the descriptions of the GI data set compilation process are fairly similar across studies, but the contributions of the different steps of the process vary widely across studies (Table 2). In the studies cited in Table 2, the following steps were included in the assignment of GI values for foods:

- 1) Identification of foods that do not contain carbohydrate or have only a minute contribution to the carbohydrate supply of the diet. These foods are assigned a GI-value of zero or they are left blank.
- 2) Identification of foods that have a direct link to a food with an analysed value (e.g. same manufacturer and same cooking method and overall description).
- 3) Identification of foods that are considered similar to a food with an analysed value (e.g. equivalent type and quantity carbohydrate and fibre, comparable preparation method such as added fat and cooking time).
- 4) Calculation of GI values based on the contribution of the carbohydrate-containing food ingredients with different GI values. This can be applied only if the recipe of the dish is known or can be reasonably estimated.
- 5) Imputation of default values (e.g. based on general knowledge of whether the GI value is expected to be low, middle, or high). This is typically applied for low GI foods (e.g. non-starchy vegetables, dairy products) or flour products.

Despite apparently similar processes in GI value derivation, the transparency of the chosen GI values and their matching with foods should be improved. Based on challenges demonstrated within EPIC (van Bakel et al. 2009b), transparency of GI information used in different countries would profit international co-operation. The ISO standard (International Organization for Standardization 2010) should be seen as a central tool in producing high-quality GI values for foods, thereby also fostering epidemiological research.

Added sugar in food composition databases

In epidemiological studies, the quantification of sugars added to foods during food preparation and processing has been challenging, since added sugar is not directly derived from chemical analysis of foods (Englyst et al. 2007). Added sugars are therefore seldom incorporated into FCDBs. Of the Nordic countries, only Norway (Norwegian Food Safety Authority et al. 2017) and Denmark (National Food Institute Denmark 2016) have estimated added sugar values in their national FCDBs. These values are based on information on food composition and ingredient food lists provided by food manufacturers. However, the process of updating the values and the completeness are not directly stated on these FCDB websites. The United States Department of Agriculture (USDA) Database for the Added Sugars Content of

Selected Foods (Pehrsson et al. 2005) was withdrawn in 2012 due to a lack of resources for updating added sugar values of constantly changing formulations of industrial food products.

Systematic descriptions of methods for deriving added sugar values for epidemiological research or public health policy purposes are few (Kelly et al. 2005, Roodenburg et al. 2011, Louie et al. 2015a). Until now, no uniform standardized methodology has existed. Common for all the methods is the concept that added sugars are a result of subtracting naturally occurring sugars from total sugars, but the contribution of objective and subjective dataset compilation steps differs widely across descriptions (Louie et al. 2015a). Similarly, in two recent reviews comparing dietary sugars intakes across countries, it has been noted that sugar definitions and the estimation methods of added sugars are inconsistent (Azais-Braesco et al. 2017, Newens and Walton 2016). These inconsistencies need to be taken into account in interpretation of epidemiological findings regarding added sugar intake and health outcomes.

Table 2. Descriptions of glycaemic index (GI) database compilation processes and contribution (%) of GI value assignment steps to overall GI database.

Reference	Country	Study	Diet method	Foods (n)	Carbohydrate zero/negligible [§]	Contribution (%)				
						Exact match	Similar food	Calculation	Imputation	Total
Flood et al. 2006	USA	CSFII ¹	DHQ (225-item)	4220	- [§]	40	20	4	36	100
Neuhouser et al. 2006	USA	WHI ²	FFQ (122-item)	350	32	-	-	-	-	100
Olendzki et al. 2006	USA	SEASONS ³	24-hour DR	1482	15	41	37	6	1	100
Martin et al. 2008	Hawaii ⁴	-	-	1592	16	11	73 [†]	-	-	100
Schakel et al. 2008	USA ⁵	-	-	2258	-	22	23	38	17	100
Similä et al. 2009	Finland	ATBC ⁶	FFQ (276-item)	1097	18	12	33	37	-	100
Aston et al. 2010	Europe	DiOGenes ⁷	Weighed 3-day FR	5105	-	19	28	-	53	100
Louie et al. 2011	Australia	MRDPP ⁸	24-hour DR	1132	24	19	48	-	9	100
Lin et al. 2012	USA	NHANES ⁹	24-hour DR	2078	13	45	32	3	7	100
Shyam et al. 2012	Malaysia ¹⁰	-	-	838	47	29	20	-	4	100
Louie et al. 2015b	Australia ¹¹	-	-	3871	29	11	46	4	10	100
Louie et al. 2016	Australia ¹²	-	-	5644	31	6	31	27	5	100
Sluik et al. 2016c	Netherlands ¹³	-	-	2556	34	24	23	6	13	100
<i>Range of database size and contribution of steps</i>					13-47	6-45	20-48	3-38	1-53	

DHQ, dietary history questionnaire; FFQ, food frequency questionnaire; 24-hour DR, 24-hour dietary recall; FR, food record; FCDB, food composition database
1 US Department of Agriculture's Continuing Survey of Food Intakes by Individuals, National Cancer Institute; 2 Women's Health Initiative Dietary Modification Trial; 3 Seasonal Variation of Blood Cholesterol Levels (SEASONS) Study; 4 Cancer Research Center of Hawaii; 5 Nutrition data system for research, University of Minnesota; 6 Alpha-Tocopherol Beta-Carotene Cancer Prevention Study; 7 Diet Obesity and Genes (DiOGenes) Study in eight European countries; 8 The Many Rivers Diabetes PreventionProject; 9 The National Nutrition and Health Examination Survey; 10 Malaysian food composition table and dietary intake calculator; 11 Australian Food, Supplement and Nutrient Database (AUSNUT 2007); 12 Australian Food Supplement and Nutrient Database (AUSNUT 2011-2013); 13 Dutch FCDB 2006, 2011
¶ Includes foods identified as unimportant in the overall carbohydrate supply of the study population.
§ Not reported or by definition excluded before assignment of GI values (all such).
† Includes calculated values.

2.2.3 FFQ VALIDITY IN MEASURING CARBOHYDRATE INTAKE

General overview

The performance of an FFQ should be evaluated in several dimensions (Willett and Lenart 2013). Firstly, the reproducibility of an FFQ refers to consistency of measurements on at least two administrations by the same person. Most commonly, reproducibility is evaluated through calculation of correlation coefficients between the two administrations. Secondly, the validity of an FFQ refers to the questionnaire measuring the dietary aspect that it is designed to measure. In validation studies, the reference method against which the FFQ is compared should have sources of error independent of the errors inherent in FFQs (Willett and Lenart 2013). Given the shortcomings of available dietary assessment methods in reliably measuring dietary intake (Table 1), validation analyses rely on alloyed gold standards. Therefore, validation studies provide information on the relative, not absolute validity (Bennett et al. 2017). This thesis focuses on the validity of FFQs.

During the past 40 years, accompanied by increased construction of new FFQs for different populations, the number of FFQ validation studies has grown substantially (Cade et al. 2004, Willett and Lenart 2013). Generally, correlation coefficients between FFQs and reference methods reach a level of 0.40 to 0.70 (Willett and Lenart 2013). FFQ design characteristics as well as the quality of validation assessments in relation to validity results have also received attention (Molag et al. 2007, Serra-Majem et al. 2009). Regarding FFQ design, it seems that comprehensive (whole diet) FFQs with more items generally perform better in ranking subjects according to their dietary intake than shorter FFQs (Molag et al. 2007). It has been suggested that the consumption frequency is the main factor in determining subject ranking (Flegal et al. 1988). However, a review on FFQ design and validation found that FFQs with self-defined portion sizes gave higher mean correlations than those with specified portion sizes or absent portion sizes (Cade et al. 2004). In their review, the analysis covered energy, fat, vitamin C and A, calcium, and iron, and cannot therefore be directly extrapolated to other dietary factors, e.g. carbohydrates. Since systematic reviews and meta-analyses of published papers in the field of nutritional epidemiology have influence on health policy, the validity of FFQs as a means of intake assessment is a dimension requiring continuous evaluation (Serra-Majem et al. 2009, Barnard et al. 2017).

Review of validation studies

Validation studies (n=19) of comprehensive (whole-diet) FFQs designed to measure the habitual long-term diet (e.g. 6-12 months) in general adult populations and reporting results for carbohydrate factors are summarized in Table 3, Section A. In general, only validation studies with at least 100 subjects living in Western food environments were included. All studies reporting validation results for dietary GI and GL (n=5) are provided in the lower part of the table (Table 3, Section B).

The design of the selected validation studies (n=19, Table 3, Section A) varied. The earliest studies included populations covering only women (Willett et al. 1985)

or men (Pietinen et al. 1988) and concerned socially and occupationally distinct populations such as professional nurses or elderly male smokers recruited from selected companies. Three out of the 19 studies utilized 24-hour DRs as the reference method (Kroke et al. 1999, Johansson et al. 2002, Sluik et al. 2016a), and one utilized a diet-history interview (Toft et al. 2008). Weighed FRs were utilized as the reference method in 30%. The number of reference days ranged from 3 (Paalanen et al. 2006, Talegawkar et al. 2015, Sluik et al. 2016a) to 28 (Willett et al. 1985, Toft et al. 2008), with 70% having a reference period of 10 days or more.

Results for total carbohydrate and fibre were reported in all 19 studies (Table 3, Section A) and showed between-method correlations in the ranges of 0.27-0.72 and 0.39-0.92, respectively. Moreover, all studies reported validation results for sugars or sucrose (correlations ranges 0.39-0.79 and 0.31-0.69, respectively). Results for starch were reported in five studies (Pietinen et al. 1988, Bingham et al. 1997, Brunner et al. 2001, McKeown et al. 2001, Marks et al. 2006), and the correlations ranged between 0.19 (Marks et al. 2006) and 0.68 (Pietinen et al. 1988). The correlation results for polysaccharides ranged from 0.57 to 0.79 (Goldbohm et al. 1994, Männistö et al. 1996, Bingham et al. 1997, Kroke et al. 1999, McKeown et al. 2001, Sluik et al. 2016a). Only one study reported a validation result for fructose (correlation coefficient 0.55) (Sam et al. 2014), and one study for lactose (correlation coefficient 0.75) (Männistö et al. 1996).

Three of the selected studies did not report any cross-classification results (Goldbohm et al. 1994, Johansson et al. 2002, Paalanen et al. 2006). In four studies, 38-41% of the subjects were classified into the same distribution quartile when averaging the results of all carbohydrate factors reported in the given study (Bingham et al. 1997, Andersen et al. 1999, Brunner et al. 2001, McKeown et al. 2001). The remaining 12 studies reported classifying 72-85% of the subjects into the same or adjacent distribution quartile (Riboli et al. 1997, Marks et al. 2006, Sam et al. 2014, Talegawkar et al. 2015) or 70-79% into the same or adjacent distribution quintile (Willett et al. 1985, Pietinen et al. 1988, Tjønneland et al. 1991, Männistö et al. 1996, Friis et al. 1997, Kroke et al. 1999, Toft et al. 2008, Sluik et al. 2016a). Gross misclassification of the subjects according to carbohydrate intakes was generally rare and ranged from 1% (Willett et al. 1985, Brunner et al. 2001) to 6% (Männistö et al. 1996).

Thus far, five FFQ validation studies have included results for dietary GI and GL (Levitán et al. 2007, Barclay et al. 2008, Murakami et al. 2008, Du et al. 2009b, Barrett and Gibson 2010) (Table 3, Section B). Regarding dietary GI, correlation coefficients ranged between 0.53 and 0.69 across these studies. The proportion of subjects classified into the same or adjacent GI distribution quintile was over 70% (Levitán et al. 2007, Barclay et al. 2008, Murakami et al. 2008). The FFQ validation study conducted as part of the EPIC study did not report cross-classification results for dietary GI or GL (Du et al. 2009b).

Regarding dietary GL, correlations between 0.60 and 0.70 were observed (Levitán et al. 2007, Murakami et al. 2008, Du et al. 2009b). However, the two Australian studies showed weaker between-method correlations for GL: 0.32 and 0.45, respectively (Barclay et al. 2008, Barrett and Gibson 2010). These two findings

were mirrored in the cross-classification results. In the study by Barclay et al. (2008), 65% of the subjects were classified into the same or adjacent dietary GL quintile based on the two methods. In the second Australian study, 49% of the subjects were correctly classified into the same tertile (Barrett and Gibson 2010). These two GL results were accompanied by slightly weaker validation results for total carbohydrate (0.48 and 0.54) than in the other three study populations (0.65-0.72) (Ocké et al. 1997, Levitan et al. 2007, Murakami et al. 2008).

To summarize, variation appears to exist in the relative validity of comprehensive FFQs in measuring different carbohydrate factors. Study design characteristics (e.g. FFQ design and quality of the reference methods), population differences, and FCDB-related issues may contribute to the observed differences between studies. This finding emphasizes the importance of validation studies as a background for epidemiological study interpretation.

Table 3. Validation studies of comprehensive FFQs measuring habitual intakes of carbohydrate factors in the general adult populations.

<i>Reference</i>	<i>Country</i>	<i>Study</i>	<i>n</i>	<i>Population</i>	<i>Age range</i>	<i>FFQ</i>	<i>Reference method</i>
<i>A. Studies reporting results for glycaemic carbohydrate, starch, polysaccharides, sugars/sucrose, and dietary fibre</i>							
Willett et al. 1985	USA	Nurses' Health Study	173	w	34-59	61-item	4*1-week FR over 1 year
Pietinen et al. 1988	Finland	Alpha-Tocopherol Beta-carotene Cancer Prevention Study	190	m	55-69	276-item	12*2-day FR over 6-months
Tjønneland et al. 1991	Denmark	-	144	m + w	40-64	92-item	2*7-day weighted FR
Goldbohm et al. 1994	Netherlands	Cohort Study on Diet and Cancer	109	m + w	55-69	150-item	3*3-day FR over 1 year
Männistö et al. 1996	Finland	Kuopio Breast Cancer Study	152	w	25-75	110-item	2*7-day FR
Bingham et al. 1997	UK	-	127	w	50-65	-	16-day weighed FR over 1 year
Frits et al. 1997	Denmark	-	122	w	20-29	178-item	3*4-day FR over 1 year
Riboli et al. 1997	Sweden	Malmö Food Study	206	m + w	50-69	350-item	6*3-day weighed FR over 1 year
Andersen et al. 1999	Norway	-	125	m	20-55	180-item	14-day weighed FR over 5 weeks
Kroke et al. 1999	Germany	EPIC	134	m + w	35-67	146-item	12*24-hour DR over 1 year
Brunner et al. 2001	UK	Whitehall II	860	m + w	39-61	127-item	7-day FR
Mc Keown et al. 2001	UK	EPIC	146	m + w	45-74	130-item	2*7-day FR
Johansson et al. 2002	Sweden	Northern Sweden Health and Disease	195	m + w	30-60	84-item	10*24-hour DR over 1 year
Paalanen et al. 2006	Finland	Health 2000 Survey	294	m + w	30-79	128-item	3-day FR
Marks et al. 2006	Australia	Nambour Skin Cancer Prevention Trial	96	m + w	25-75	129-item	12 days weighed FR over 1 year
Toft et al. 2008	Denmark	Inter99	264	m + w	48 avg	198-item	28-days diet history interview

Table 3 (continued)

<i>Reference</i>	<i>Country</i>	<i>Study</i>	<i>n</i>	<i>Population</i>	<i>Age range</i>	<i>FFQ</i>	<i>Reference method</i>
Sam et al. 2014	New Zealand	-	132	m + w	30-59	154-item	4*2-day weighed FR over 1 year
Talegawkar et al. 2015	Columbia	Baltimore Longitudinal Study of Ageing	468	m + w	26-95	-	3-day FR
Sluik et al. 2016	Netherlands	Nutrition questionnaires plus	376	m + w	25-69	160-item	1-5*24-hour DR (mean 2.7)
<i>B. Studies reporting results for dietary glycaemic index and dietary glycaemic load</i>							
Levitan et al. 2007	Sweden	-	141	m	40-74	96-item	2*1-week FR 6 months apart
Barclay et al. 2008	Australia	Blue Mountains Eye Study	78	m + w	65-85	145-item	3*4-day weighed FR over 1 year
Murakami et al. 2008	Japan	-	184	m + w	31-76	150-item [¶]	4*4-day FR over 1 year
Du et al. 2008 [§]	Netherlands	EPIC	121	m + w	23-72	79-item	12*24-hour DR over 1 year
Barrett and Gibson, 2010	Australia	-	72	m + w	23-72	297-item	4*7-day FR over 1 year

FFQ, food frequency questionnaire; FR, food record; DR, dietary recall; m, men; w, women; EPIC, European Prospective Investigation into Cancer and Nutrition; Inter99, Danish population-based randomized intervention study.

[¶] Diet history questionnaire focusing on the previous month and repeated four times over a 1-year period.

[§] Validation results for total carbohydrate in this study population are reported in Ocké et al. 1997.

2.3 CARBOHYDRATES IN MODERN DIETS

2.3.1 GENERAL TRENDS

On the global level, food consumption has changed from less processed plant-based staple foods to more refined and processed carbohydrate food sources, thereby manifesting as a global nutrition transition (Mattei et al. 2015). In Europe between 1961 and 2001, the availability of fruits and vegetables and the share of energy from vegetable products have increased markedly (Schmidhuber and Traill 2006). Per capita sugar consumption in the Mediterranean area, Belgium, and France has increased since the 1960s, whereas in UK, Ireland, and Northern Europe a decrease has been observed. These food balance sheet-based observations need confirmation from individual food consumption data since food losses are not taken into account in food balance sheet-based analyses.

According to the European Food Safety Authority (EFSA), in European working-aged adults the average carbohydrate intake ranged from 37.9 E% (Greece, men) to 53.9 E% (Czech Republic, women), sucrose intake from 7.6 E% (Hungary, men) to 13.7 (Norway, women), and dietary fibre intake from 15.7 g/day (France, women) to 29.7 g/day (Poland, men) (EFSA 2010). In a recent review concerning national surveys of selected European countries, added sugar intakes ranged from 7.3 E% (adults, Norway) to 11.4 E% (NMES, UK adults) (Azais-Braesco et al. 2017). On the global level, young adults in USA and New Zealand have the highest intakes of added sugar (16.3 E%) (Newens and Walton 2016). However, due to different survey designs, dietary assessment methods (including non-uniform food coding and classification systems), and not least the different ways of estimating added sugar, comparisons between countries should be evaluated cautiously.

Dietary patterns of developed countries, including USA, Australia, France, Denmark, and the Netherlands, have been found to converge with regard to the contribution of the main food groups to energy and nutrient intakes (Auestad et al. 2015). The EPIC Study has demonstrated that northern and southern European countries have differences in the consumption of carbohydrate-providing food groups. For example, fruit and vegetable consumption was higher in southern Europe than in northern Europe (Cust et al. 2009). These differences were reflected in the average dietary GL estimates in these countries, but average dietary GI appeared to vary only modestly across Europe (van Bakel et al. 2009a).

According to the cross-sectional FINDIET surveys, the contribution of carbohydrates to energy intake has, on average, decreased in the Finnish adult population, especially between 2007 and 2012 (Figure 1). During the same time period sucrose intake (E%) has remained unchanged in both sexes, and fibre intake (g/day) has decreased in men (Figure 2). The consumption of fruits and vegetables has increased, and consumption of potatoes and cereals (especially rye) has decreased during 2007-2012 (Raulio et al. 2013, National Nutrition Council 2014).

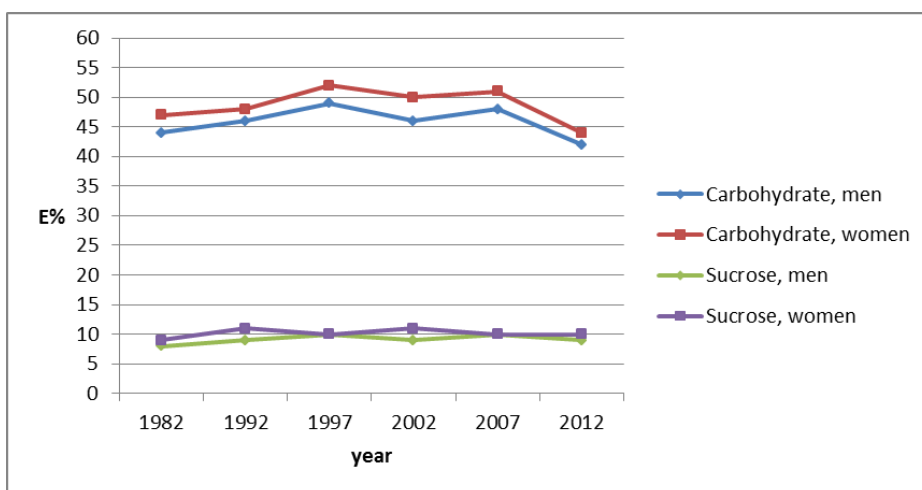


Figure 1 Intake of carbohydrate (E%) and sucrose (E%) in Finnish 25–64-year-old adults between 1982 and 2012. The National FINDIET Surveys are based on cross-sectional data (Uusitalo et al. 1987, Kleemola et al. 1994, Anttolainen et al. 1998, Männistö et al. 2003, Paturi et al. 2008, Helldán et al. 2013). Due to varying dietary assessment methods and survey designs in terms of the included study areas, the results from different years may not be fully comparable.

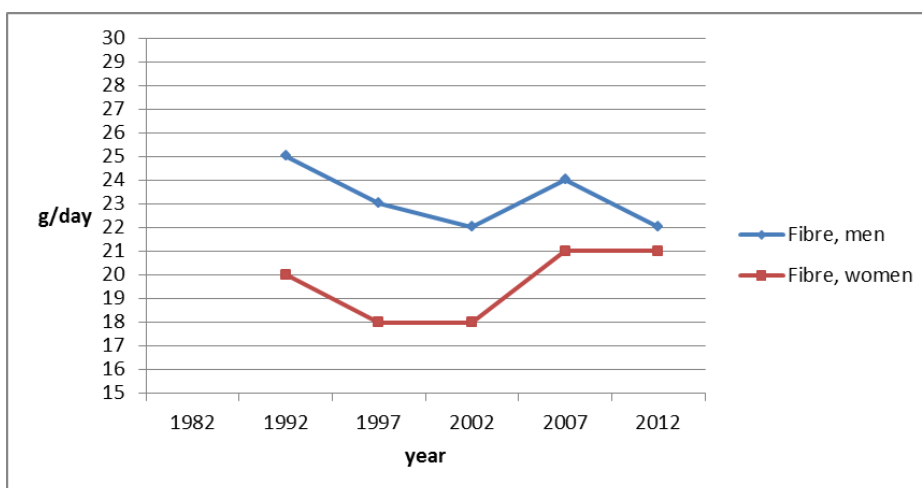


Figure 2 Intake of dietary fibre (g/day) in Finnish 25–64-year-old adults between 1992 and 2012. The National FINDIET Surveys are based on cross-sectional data (Kleemola et al. 1994, Anttolainen et al. 1998, Männistö et al. 2003, Paturi et al. 2008, Helldán et al. 2013). Due to varying dietary assessment methods and survey designs in terms of the included study areas, the results from different years may not be fully comparable.

2.3.2 CARBOHYDRATES IN NUTRITION RECOMMENDATIONS

Nutrition recommendations represent an instrument to steer nutrition and health policy, and provide the background against which nutritional surveillance is assessed, and epidemiological research findings are interpreted (Nordic Council of Ministers 2014). Factors affecting recommendations include population health behaviour and challenges and a growing body of scientific evidence on relationships between nutritional exposures and health outcomes. Differences in recommendations set by health authorities and scientific communities arise from different methodological approaches. These include the selection of exposures and outcomes, the identification of source materials, and applied data quality assessments. The implementation of recommendations into practical guidelines for the general public is affected by the food cultures of the target populations (Buyken et al. 2018).

Nutrition recommendations of global, European, and Nordic health authorities are generally congruent with regard to the recommended level of carbohydrates (EFSA 2010, Nordic Council of Ministers 2014, WHO 2003) (Table 4). The Finnish national nutrition recommendations have been consistent over time (National Nutrition Council 2014). The upper limit of total carbohydrate intake in the WHO recommendation is higher than in the Nordic recommendation. This reflects the international perspective of the WHO in prompting nutritionally adequate diets for populations in different stages of nutrition transition. Overall, high carbohydrate intake coupled with high fibre intake represents a central means to achieve adequate levels of protective nutrients and promote health. The recommendations also include food-based dietary guidelines. For example, high daily intakes of vegetables, fruits and berries, favouring of high-fibre whole-grain products, and avoiding regular consumption of SSB and other sweetened food products are recommended in Finland and the Nordic countries (National Nutrition Council 2014, Nordic Council of Ministers 2014). Population health is promoted by decreasing energy density, increasing nutrient density, and improving carbohydrate quality.

The rationale for inclusion of upper limit values for free or added sugar in the recommendations has been questioned in part because the simultaneous achievement of both sugar and fat recommendations has been suggested to be difficult in practice (Erickson and Slavin 2015, Sadler et al. 2015), and in part because a uniform assessment method for free or added sugar is currently lacking (Azais-Braesco et al. 2017). In their scientific opinion EFSA did not set an upper limit for sugar (EFSA 2010). The reasoning was that evidence for adverse health effects of sugars per se was regarded as insufficient, and rather attributable to an overall unbalanced dietary pattern (e.g. high intake of SSB). The WHO has based its free sugar recommendation on evidence mainly accumulated from (short-term) randomized controlled trials and epidemiological studies with SSB or other sugar-containing foods as the predominant exposures (WHO 2015). The conditional recommendation not to exceed free sugar intake of 5 E% was predominantly based on studies related to dental health. The UK Scientific Advisory Committee on Nutrition (SACN) has emphasized in its recent report the achievement of a healthy diet with regard to dietary carbohydrates simultaneously with the strict 5 E% recommendation for free sugar (Scientific Advisory Committee on Nutrition 2015).

Table 4. *Examples of recommended carbohydrate intakes for adult populations.*

<i>Recommendation</i>	<i>Authority</i>	<i>Year</i>	<i>Carbohydrate (E%)</i>	<i>Sugar (E%)</i>	<i>Fibre (g/day)</i>
Finland	National	1987	>50	max. 10 ¹	30-35
	Nutrition	1998	55-60	max. 10 ^{1,2}	25-35
	Council	2005	50-60	max. 10 ¹	25-35
		2014	45-60	<10 ¹	25-35
Nordic countries	Nordic Council of Ministers	2012	45-60	<10 ¹	25-35
Europe	EFSA	2009	45-60	-	>25
WHO	WHO	2003	55-75	<10 ³	>25
		2015	-	<10 / max. 5 ³	-
UK	SACN	2015	50	max. 5 ³	30

¹ Added sugar

² For adults with daily energy requirements below 8 MJ

³ Free sugar

References: National Nutrition council 2014, Nordic Council of Ministers 2014, EFSA 2010,

WHO 2003, WHO 2015, Scientific Advisory Committee on Nutrition 2015

2.3.3 SUGAR INTAKE AND DIET QUALITY IN ADULTS

Sugar is regarded as a carbohydrate factor that negatively affects the nutrient density of the diet. This issue, also called the nutrient dilution hypothesis, has been approached through studying the association between added sugar and micronutrient intakes. However, two review articles published in 2007 suggested that no firm conclusions on the negative association between added sugar and micronutrient dilution could be drawn (Gibson 2007, Rennie and Livingstone 2007). Both reviews referred mainly to studies in children and older adults. More studies being conducted and published in these population groups is justified since children and older adults are at higher risk of low nutrient density due to low energy intake requirements than working-aged adults.

Methodological challenges that might contribute to the contradictory results obtained in this study area include the heterogeneous definitions of sugars (e.g. total sugars vs added sugar), inconsistent approaches to energy adjustment, and the applied criteria for micronutrient adequacy (Livingstone and Rennie 2009). It is also noted that misreporting (e.g. energy underreporting and selective misreporting of certain food groups) was not sufficiently taken into account in studies. A recent systematic review including studies in both adults and children found mainly negative associations between added sugar and micronutrient intakes in energy-adjusted analyses. (Louie and Tapsell 2015). However, the strength of the observed associations was mostly small to moderate, thereby casting doubt on their clinical significance.

Added sugar intake in relation to macronutrient and fibre intake

The systematic review of Louie and Tapsell (2015) was used as a basis for the literature search for this thesis. Studies focusing on association between added sugar intake and macronutrients and dietary fibre in the general adult population (excluding children, adolescents, patient groups, and populations of exclusively older adults) are summarized in Table 5. All studies were cross-sectional. The exact methods used to estimate added sugar intake were mostly not described in detail. Moreover, some of the studies used an adjustment for total energy intake (mostly E%), while others used absolute intakes (g/day). The latter may introduce confounding to the association between added sugar and other nutrients due to body size and metabolic efficiency of the subjects (larger individuals tend to have higher intakes of all nutrients due to their energy requirements, compared to smaller individuals). It is also noted that the majority of the studies on the association between sugar and macronutrients or fibre (12 out of 16 studies) were published in the 1990s.

Despite heterogeneous definitions of sugar, a consistent inverse relationship between sugar and fat on the basis of energy-adjusted analyses (E%) has been demonstrated in the selected studies (Table 5), as well as in another systematic review (Sadler et al. 2015). Regarding the association between energy-adjusted sugar (E%) and dietary fibre intake, a positive association was evident when using total sugars (Gibney et al. 1995), or sucrose (Linseisen et al. 1998) as the exposure. In contrast, large population-based studies with over 10 000 subjects across continents have mainly found negative associations between added sugar and dietary fibre (Lewis et al. 1992, Bolton-Smith and Woodward 1995, Bowman 1999, Cobiac et al. 2003, Marriott et al. 2010). These contrasting findings may indicate a confounding due to the fact that fruits and vegetables are a central source of both fibre and sugars (e.g. sucrose). Therefore, it seems justified to seek for methods to reliably estimate added sugar intakes when studying the effect of sugar intake on diet quality (Louie and Tapsell 2015). Overall, relative intake of added sugar (E%) was studied in 9 out of 16 studies (Table 5). Negative associations with intake of fat (E%) (7 studies), protein (E%) (4 studies), natural or intrinsic sugars (E%) (2 studies) were reported. Furthermore one study reported a positive association between added sugar and carbohydrate intake (E%) (Lewis et al. 1992). These associations represent the mathematical dependency of the macronutrients (carbohydrate, fat, protein) in an energy-adjusted modelling approach (Sadler et al. 2015). In addition, such associations suggest that there are differences in the food composition of diets with varying relative added sugar levels.

Added sugar intake in relation to food intake and diet quality

Another approach to investigate the association of added sugar and diet quality is to study the relationship between sugar intake and food choices or diet quality indices or patterns. Table 6 shows 10 studies including predominantly adult populations. None of the selected studies had a prospective design.

Several studies found lower intakes of cereals, cereal products, or grains in adults with high added sugar intake expressed as E% (Bowman 1999, Britten et al. 2000,

Cobiac et al. 2003). In an Australian survey, adults in the highest deciles of added sugar were found to consume less wholemeal bread than those in the lowest deciles, which was reflected in the lower fibre intake in high added sugar consumers (Baghurst et al. 1992). Fairly consistently, the consumption of vegetables, fruits, and milk has been shown to decrease with increasing intakes of added sugar in American (Lewis et al. 1992, Bowman 1999, Britten et al. 2000) and Australian (Baghurst et al. 1992, Cobiac et al. 2003) studies. Similar findings have also been reported in the UK and France (Emmett and Heaton 1995, Drewnowski et al. 1997). In one study without adjustment of total energy, a positive association between sugar and fruit intake was observed, suggesting that total sugars instead of added sugar was the studied variable (MacIntyre Una et al. 2012).

Regarding meat consumption, the findings were mixed. An early Australian study with 1848 adults aged 18+ years did not find an association between added sugar and meat or poultry consumption (Baghurst et al. 1992), whereas another study showed an inverse relationship between added sugar and meat consumption in a sample of 14709 Americans (Bowman 1999). A nationally representative large sample (n=10 417) of Australian adults showed a positive association between added sugar (E%) and meat consumption in men, and the opposite in women (Cobiac et al. 2003). A negative association between added sugar and fish intake was reported in one American study (Bowman 1999).

The four studies investigating the association between added sugar and dietary indices or patterns had varying designs (Table 6). The Val-de-Marne Study in 837 French adults showed that sucrose intake was associated with higher dietary variety score (higher number of different foods in all food categories), and that dietary diversity (higher number of consumption occasions from the major food groups) was high regardless of sucrose intake (Drewnowski et al. 1997). However, sucrose intake in France at that time was low, accounting for 6.5 E%. In a study in UK, NMES E% was inversely associated with the “health-conscious” dietary pattern in both sexes when the a posteriori principal component analysis method was applied (Gibson and Ashwell 2011).

Two studies reported on associations between added sugar and healthy diet adherence using a priori indices/scores. A Dutch survey applying the Dutch Healthy Diet Index with 10 components found no indications of diet quality differences when comparing adults adherent and non-adherent to the added sugar (<10 E%) or free sugar (<5 E%) recommendations (Sluik et al. 2016b). In that study, when score components were explored separately, subjects adhering to the recommendations scored higher for dietary fibre, vegetables, fruit, and fish, but lower for saturated fat than non-adherent subjects. A representative sample of Americans found that in subjects with low energy intakes, added sugar was associated with lower scoring on the Healthy Eating Index, but in subjects with higher energy intakes the association between added sugar and healthy eating was inconsistent (Britten et al. 2000).

Summary of added sugar intake and diet quality in adults

Overall, research on added sugar intake and diet quality faces methodological challenges, including non-uniform definitions of sugars and food group classifications, both of which are dependent on the FCDBs. Moreover, spurious differences across findings may originate from methodological choices, including energy-adjustment and consideration of misreporting. Regarding macronutrients, added sugar represents an energy source displacing other energy-yielding nutrients, especially fat. Thus far, the majority of population-based studies suggest that high added sugar intake is associated with low dietary fibre intake. These kinds of changes in dietary composition may have implications for long-term population health. Findings of the relationship between added sugar intake and food consumption or dietary patterns remain mixed. However, the majority of studies show an inverse relationship between added sugar and intake of vegetables and fruit. Further studies investigating the association between added sugar intake and diet quality in free-living adult populations are needed. This is especially important due to the changing food environment. Such studies from Nordic countries are lacking.

Table 5. *Studies reporting associations between sugar and macronutrient intakes in adult populations.*

<i>Reference</i>	<i>Country, Study</i>	<i>Population</i>	<i>Exposure</i>	<i>Dietary method</i>	<i>Results</i>
Baghurst et al. 1992	Australia, -	1848, m+w, aged 18+	Added sugar, E% (deciles)	FFQ	Fat (E%), protein (E%), natural sugars (E%), fibre (g/day): ↓ No adjustments for other variables.
Lewis et al. 1992	USA, Nationwide Food Consumption Survey	17 047 m+w, aged 19+	Added sugar, E% and g/kg body weight (percentiles)	1- to 3-day FR	Fat (E%) and protein (E%): ↓ Total carbohydrate (E%): ↑ No adjustments for other variables.
Baghurst et al. 1994	Australia, -	2150 m+w, aged 18+	Fat, E% (quintiles)	FFQ	Total carbohydrate (E%): ↓ Simple and natural sugars (E%): ↓ Added sugars (E%): ↓ (men only) No adjustments for other variables.
Bolton-Smith and Woodward 1994	UK, Scottish Heart Health and MONICA Studies	11 626 m+w, aged 25-64	Extrinsic sugar, E%	FFQ	Intrinsic sugar (E%), starch (E%), fat (E%), protein (E%), and alcohol (E%): ↓ Energy intake: ↑ No adjustments for other variables.
Emmett and Heaton 1995	UK, -	160 m+w	Extrinsic sugar, E%	4-day weighed FR	Fat (E%): ↓ Adjustment for energy under-reporting did not affect result.
Bolton-Smith and Woodward 1995	UK, Scottish Heart Health and MONICA Studies	11 626 m+w, aged 25-64	Extrinsic sugar, E%	FFQ	Fibre (g/day): ↓ Adjustments: age, smoking, total energy intake, alcohol consumption, weight, height
Gibney 1995	USA, Nationwide Food Consumption Survey	8296 m+w, aged 19+	Total sugars excl. lactose/4.18 MJ (percentiles)	3-day FR, household-level	Fat (g/day), protein (g/day), SAFA (g/day): ↓ Total carbohydrate (g/day): ↑ Fibre (g/day): ↑ (adults 51+ years) No adjustments for other variables

Table 5 (continued)

<i>Reference</i>	<i>Country, Study</i>	<i>Population</i>	<i>Exposure</i>	<i>Dietary method</i>	<i>Results</i>
Gibson 1996	UK, Dietary and Nutritional Survey of British Adults	2197 m+w	Non-milk extrinsic sugar, E% (quintiles)	7-day weighed FR	Fat (E%), SAFA (E%), MUFA (E%), n-3 PUFA (E%), and n-6 PUFA (E%): ↓ No adjustments for other variables
Flynn et al. 1996	Ireland, -	83 w, aged 10-55	Total added sugars, g/day and E%	7-day dietary history	Fat (E%): ↓ (both for exposure in g/day and E%) No adjustments for other variables
Drewnowski et al. 1997	France, Val-de-Mame Study	837 m+w, aged 18+	Added sucrose, g/1000 kcal (deciles)	Diet history interview	Fat (g/day): ↓ Fat (E%): NS No adjustments for other variables.
Linseisen et al. 1998	Germany, German National Food Consumption Survey	15 838 m+w, aged 4+	Sucrose, g/day	7-day FR	Fat, SAFA, MUFA, PUFA, protein, polysaccharides, alcohol: ↓ Dietary fibre: ↑ Adjustments: energy (several models), age, sex
Bowman et al. 1999	USA, Continuing Survey of Food Intake by Individuals	14 709 m+w, aged 2+	Added sugars, E%	24-hour DR	Fat (g/day) and SAFA (g/day): NS Protein (g/day), fibre (g/day), fat E% (tendency): ↓ Total carbohydrate (g/day): ↑ No adjustments, but the effect of age, race and income is discussed
Cobiac et al. 2003	Australia, National Nutrition Survey	10 417 m+w, aged 19+	Added sugars, E% (tertiles)	24-hour DR	Protein (E%), natural sugars (E%), starch (E%), fibre (g/1000 kJ): ↓ No adjustments for other variables.

Table 5 (continued)

<i>Reference</i>	<i>Country, Study</i>	<i>Population</i>	<i>Exposure</i>	<i>Dietary method</i>	<i>Results</i>
Parnell et al. 2008	New Zealand, National Nutrition Survey	4636 m+w, aged 15+	Sugars and sucrose, g/day and E%	24-hour DR	Fat (E%): ↓ No adjustments for other variables
Mariott et al. 2010	USA, National Health and Nutrition Examination Survey	15 189 m+w, aged 4+	Added sugar, E%	Two 24-hour DR (usual intake: NCI-method)	Fibre (g/day): ↓ Adjustment: total energy intake
McIntyre et al. 2012	South Africa, -	1742 m+w, aged 15-65	Sugars, g/day	FFQ	Daily energy, protein (g/day), fat (g/day), total carbohydrate (g/day), fibre (g/day): ↑ Alcohol (g/day): ↓ No adjustments with other variables

FFQ, food frequency questionnaire; FR, food record; DR, dietary recall; E%, percentage of total energy; m, men; w, women; Associations: ↑ =positive, ↓ =negative, NS=non-significant; MONICA, Multinational Monitoring of trends and determinants in Cardiovascular disease; SAFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

Table 6. Studies reporting associations between added sugar and food groups, dietary patterns or healthy diet indices in adult populations.

Reference	Country	Population	Exposure	Dietary method	Results
Baghurst et al. 1992	Australia, -	1848, m+w, aged 18+	Added sugars, E% (deciles)	FFQ	Cookies, cakes, flavoured milk, chocolate, jams, honey, sugar as such, soft drinks: ↑ Whole meal bread: ↓ Meat/poultry: NS
Lewis et al. 1992	USA, Nationwide Food Consumption Survey	1707 m+w, aged 19+	Added sugars, %E and g/kg body weight (percentiles)	3 days (household level)	Grains, sweets, non-alcoholic beverages: ↑ Milk, vegetables, fruit (tendency): ↓
Emmett and Heaton 1995	UK, -	1715 m+w, aged 25-69	Extrinsic sugars, E%	FFQ (carbohydrate-specific)	Biscuits, cakes, puddings, confectionery, potatoes with fat: ↑ Fruit: ↓ Potatoes without fat, vegetables: NS
Drewnowski et al. 1997	France, Val-de-Marne Study	837 m+w, aged 18+	Added sucrose, g/1000 kcal (deciles)	Diet history interview	Dietary diversity score: NS (close to maximum across added sucrose deciles) Dietary variety score: ↑ Confectionery, sweets: ↑ Vegetables, alcohol (tendency): ↓ Fruit: NS
Bowman et al. 1999	USA, Continuing Survey of Food Intake by Individuals	14 709 m+w, aged 2+	Added sugars, E%	24-hour DR	Grains, fruit, vegetable, meat, poultry, fish; fruit juices, fluid milk (tendency): ↓ SSBs, cakes, cookies, milk desserts, and candies: ↑ Dairy: NS No adjustments. Effect of age, race, and income discussed.
Britten et al. 2000	USA, Continuing Survey of Food Intake by Individuals	15 011 m+w, aged 2+	Added sugar, (teaspoons)	24-hour DR	Healthy diet (Healthy Eating Index): ↓ (in subjects with low energy intake) Healthy diet (Healthy Eating Index): NS (in subjects with high energy intake) Fruit: ↓ (in subjects over-consuming energy) Fruit, vegetable, milk, and grains: ↓ (in subjects not over-consuming energy) No adjustments, but the effects of age and sex were discussed.

Table 6 (continued)

Reference	Country	Population	Exposure	Dietary method	Results
Cobiac et al. 2003	Australia, National Nutrition Survey	10417 m+w, aged 19+	Added sugars, E% (tertiles)	24-hour DR	Cereals, fats and oils, fruit and vegetable products, meat products (women), alcoholic beverages (men): ↓ Non-alcoholic beverages, sugar products, confectionery, meat products (men): ↑ No adjustments for other variables
Gibson and Ashwell 2011	UK, National Diet and Nutrition Survey	1724 m+w, aged 19-64	Non-milk extrinsic sugars, E%	7-day weighed FR	“Health-conscious” pattern: ↓ “Bread, spread and cheese” pattern: ↓ (men) “Cakes, sugar and beverages” pattern: ↑ (men) “Soft drinks and savoury snacks”, “beverages milk and sugar” and “red meat avoiders” patterns: ↑ (women) Adjustments: age
MacIntyre Una et al. 2012	South Africa, -	1742 m+w, aged 15-65	Sugars, g/day (quartiles)	FFQ	Bread, sugar, soft drinks: ↑ Fruit, vegetables ↑ (men) Maize meals: ↓ No adjustments for other variables
Sluik et al. 2016	Netherlands, Dutch National Food Consumption Survey	3817 m+w, aged 7-69	Added sugars, E%, Free sugars, E%	2*24-hour DR (usual intake, Multiple Source Method)	<i>Adherence to the free or added sugar recommendations:</i> Diet quality (Dutch Healthy Diet Index): NS <i>Component scoring in subjects adherent to the sugar recommendations compared to non-adherent subjects:</i> Dietary fibre, vegetables: ↑ (<5 E% free sugar) SAFA, alcohol: ↓ (<5 E% free sugar) Fruits, fish: ↑ (<10 E% free sugar)

FFQ, food frequency questionnaire; FR, food record; DR, dietary recall; E%, percentage of total energy; m, men; w, women; Associations: ↑ =positive, ↓ =negative, NS=non-significant; SAFA, saturated fatty acids.

2.4 DIETARY CARBOHYDRATES AND HEALTH

During the past years several systematic reviews dealing with the relationship of carbohydrate intake (both nutrient and food group level factors) and health outcomes have been published both in Nordic countries (Sonestedt et al. 2012, Fogelholm et al. 2012, Overby et al. 2013) and in central Europe (Hauner et al. 2012, Scientific Advisory Committee on Nutrition 2015). These reviews were conducted to inform health authorities in setting nutrition recommendations. Both of the systematic reviews from central Europe included detailed evidence from randomized controlled trials and cohort studies in both adults and children. In both reviews, the studied carbohydrate factors were highly detailed and included total carbohydrates, mono- and disaccharides, dietary fibre, and GI (Hauner et al. 2012, Scientific Advisory Committee on Nutrition 2015). Moreover, the scope of the studied health outcomes and related risk factors was comprehensive (Table 7). This thesis concentrates on the relationship between carbohydrate factors and obesity in light of the prospective cohort studies conducted in the general adult population. The SACN report dealing with carbohydrates and health was used as a basis for the literature search of this thesis (Section 2.4.2). In addition, observational data from cross-sectional studies are reviewed, especially when only few longitudinal studies were available.

Table 7. *Health outcomes and related risk factors studied in relation to carbohydrate intakes (modified from Scientific Advisory Committee on Nutrition, 2015).*

<i>Health outcomes</i>	<i>Related risk factors</i>
Cardiovascular diseases Type 2 diabetes mellitus	Blood pressure Fasting blood lipid concentrations Coronary and vascular factors Inflammatory markers Body weight and body composition (=obesity) Glycaemia, insulinaemia, insulin resistance
Colorectal cancer	Colorectal adenomas and function

2.4.1 OBESITY

Obesity refers to a state in which excess fat has accumulated in the body of an individual to an extent that it poses a health risk (WHO 2000). Obesity is inherently a multifactorial phenomenon dependent on both genetic and environmental factors. When energy intake chronically exceeds energy expenditure, excess fat accumulates both subcutaneously and viscerally i.e. fat in and around cells of the inner organs and muscles. Both number and size of the adipocytes increases (de Ferranti and Mozaffarian 2008). Metabolic and cardiovascular complications associated with obesity are related foremost to the accumulation of visceral fat (Huxley et al. 2010). As an important energy store, adipose tissue participates in macronutrient

homeostasis. On the other hand, increased fat stores render and maintain a systemic low-grade inflammatory milieu which promotes further metabolic abnormalities (Forsythe et al. 2008). These include dyslipidaemia, hyperglycaemia, insulinaemia, and elevated blood pressure. Obesity is thus regarded as an important risk factor for non-communicable diseases including cardiovascular diseases and type 2 diabetes mellitus (WHO 2000).

In epidemiological research, adiposity can be defined in several ways. One of the most widely used indicators of general adiposity or body size in adults is body mass index (BMI, calculated as weight divided by squared height, kg/m^2) (WHO 2000). Classification of body size according to BMI includes the following categories: underweight (BMI < 18.5), normal weight (BMI 18.5-24.9), overweight (BMI 25.0-29.9), obese (BMI 30.0-39.9), and morbidly obese (BMI \geq 40.0). As an obesity measure, BMI does not take into account the distribution of adipose tissue or the amount of lean body mass.

Abdominal obesity is assessed by measuring the waist circumference (WC, cm). The cut-off points to classify presence of abdominal obesity are set sex-specifically, and ethnic-specific cut-offs have been recommended (Alberti et al. 2009). For Caucasians, cut-offs indicating increased risk and substantially increased risk of chronic diseases are for men WC > 94 cm and WC > 102 cm and for women WC > 80 cm and WC > 88 cm, respectively (WHO 2008). In Finland, cut-off values of WC > 100 cm in men and WC > 90 cm in women are recommended for use in clinical practice (Working group of the Finnish Medical Society Duodecim and the Finnish Association for the Study of Obesity 2013).

Prevalence and trends

Globally, between 1975 and 2014, the prevalence of adult obesity has increased from 3.2% to 10.8% in men, and from 6.4% to 14.9% in women (NCD Risk Factor Collaboration 2016). That review also found that in 2014, the obesity prevalence (BMI \geq 30 kg/m^2) level of 30% was reached in both men and women in high-income English-speaking countries.

In Finland, based on cross-sectional FINRISK studies, the prevalence of obesity (BMI \geq 30 kg/m^2) in working-aged adults increased during 1992-2007 from 18.8% to 21.9% in men and from 18.2% to 20.1% in women (Lahti-Koski et al. 2012). Between 2007 and 2012, obesity prevalence did not change, but remained at a high level (20.3% and 20.0% in men and women, respectively) (Männistö et al. 2015). This suggested a levelling off in rising obesity prevalence rates. It is noted, however, that during the 1990s, when a moderate increase was seen in mean BMI, an adverse development towards higher mean WC values occurred in the Finnish general population (Lahti-Koski et al. 2007). According to FINRISK 2012 Study, the prevalence of abdominal obesity in 25 to 64 year-olds remained high, at 31%, in both sexes (Männistö et al. 2015). In the Health 2011 Survey, over 40% of Finnish men and women aged 30 years and over were abdominally obese. This showed that obesity was more common in the older age groups (Lundqvist et al. 2012).

In addition to Finland, apparent levelling off of the increasing BMI-based obesity prevalence has also been reported in at least the American population (Flegal et al.

2012). It has been suggested that the use of BMI as the predominant obesity measure masks the continuum of the obesity epidemic (Visscher et al. 2015). As possible explanations, these authors discussed the role of decreasing participation rates in surveys, lack of representative samples, and the use of self-reported rather than measured obesity values. Overall, despite apparent levelling off, obesity prevalence remains at levels that are unsatisfactory from the public health perspective leaving room for preventive actions and warranting more scientific research on obesity.

2.4.2 CARBOHYDRATE FACTORS AND OBESITY

Mechanisms

In essence, obesity is a result of a long-term imbalance between energy intake and energy expenditure. Figure 3 illustrates metabolic pathways that potentially link carbohydrate factors to obesity development (Slavin 2005, Aller et al. 2011). The effects of carbohydrate-containing foods on the glycaemic response and its consequences on food intake regulation are seen as central (Ludwig 2002). In recent times, the special role of fructose in obesity aetiology has received much attention (Stanhope 2016). Moreover, the effect of dietary sugars on the reward circuitry of the brain, and their cross-talk with colonic microbiota represent further approaches to elucidating the link between sugars and obesity-related metabolic phenomena (Ochoa et al. 2015, Lambert et al. 2017). In a broader view, overall food intake and therefore also intake of carbohydrate-containing foods are affected by environmental factors such as social and cultural circumstances (Gordon-Larsen 2014). Thus, carbohydrate factors may be associated with obesity through several simultaneous mechanisms.

Epidemiological evidence from cohort studies

Table 8 summarizes 17 prospective studies that have investigated the relationship between obesity and carbohydrate factors in adult populations. The carbohydrate factors include carbohydrate (total/glycaemic), dietary fibre, sucrose, and dietary GI and GL. No cohort studies investigating the association between monosaccharides or disaccharides, beyond sucrose, and obesity were identified. Moreover, no cohort study used free or added sugars from all food sources as the exposure measure. Follow-up times ranged from 1 to 12 years, with 14 studies having at least a 4-year follow-up. In 60% of the studies, dietary assessment relied on FFQs. The majority of studies (12 out of 17) used weight change as the obesity outcome (Table 8). Five studies used WC change as the outcome representing abdominal obesity (Koh-Banerjee et al. 2003, Halkjaer et al. 2006, Hare-Bruun et al. 2006, Du et al. 2009a, Du et al. 2010). One study used WC adjusted for BMI as a proxy measure for visceral adiposity (Romaguera et al. 2010).

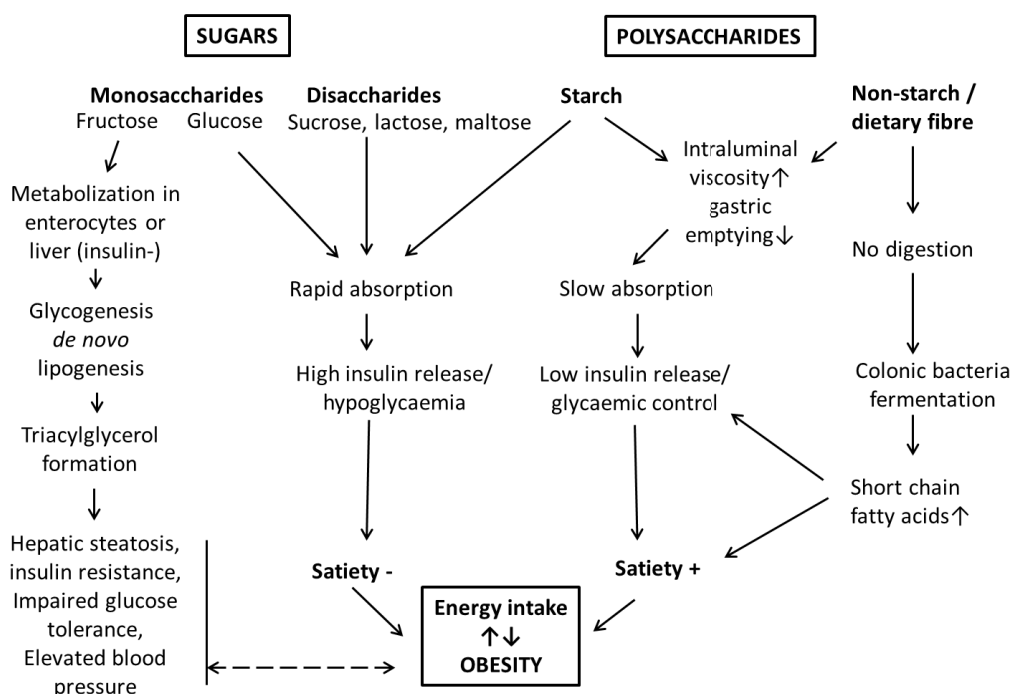


Figure 3 Main physiological effects of dietary carbohydrates with regard to obesity. (modified from Slavin 2005 and Aller et al. 2011)

Total carbohydrate

A cross-sectional study in 11 626 Scottish adults found an inverse relationship between total carbohydrates and obesity based on BMI (Bolton-Smith and Woodward 1994). Similarly, a Canadian study with 4451 participants reported a 40% lower likelihood of being obese in the highest carbohydrate intake quartile compared with the lowest quartile (Merchant et al. 2009). Regarding BMI, a one-year follow-up of 572 American adults showed no association between total carbohydrate intake and obesity occurrence (Ma et al. 2005).

Of the cohort studies that used weight or weight change as the outcome, two revealed an inverse association between carbohydrates and obesity. These were the Nurses' Health Study (NHS) with 31 940 subjects (Colditz et al. 1990) and the Coronary Artery Risk Development in Young Adults Study (CARDIA) Study with 2909 young adults (Ludwig et al. 1999). In contrast, most of the smaller prospective studies reported no significant associations (Haffner et al. 1991, Parker et al. 1997, Iqbal et al. 2006). One early Finnish study showed a positive association between carbohydrate intake and body weight in women (relative risk: 1.71, 95% confidence interval (95% CI): 1.0-2.6 for highest vs. lowest quintile), but not in men (Rissanen et al. 1991).

Regarding abdominal obesity, the CARDIA Study (n=2909) did not observe an association between carbohydrate intake and waist-to-hip ratio (Ludwig et al. 1999), nor was an association evident in the Danish Diet and Cancer cohort that included 42 696 middle-aged adults (Halkjaer et al. 2006). However, Halkjaer et al. reported a significant positive association between carbohydrates originating from refined grains, potatoes, and foods with simple sugars, and WC change. In contrast, they observed an inverse association between the intake of fruit- and vegetable-originating carbohydrates and WC change. These food source-related findings were statistically significant only in women (Halkjaer et al. 2006). Comparable to the overall null result in the Danish Diet and Cancer Cohort, no association between carbohydrate intake and visceral adiposity was evident in the EPIC Study with 48631 Europeans (Romaguera et al. 2010). To summarize, while total carbohydrate intake was not found to be consistently associated with obesity outcomes in the general adult population, the food source of the carbohydrate seems to be important.

Sugars

Some meta-analyses have investigated the relationship of free sugar or SSB consumption and obesity measures (Te Morenga et al. 2013, Malik et al. 2013). Both the cited meta-analyses were based on cohort studies and randomized controlled trials in children and adults, and came to the conclusion that SSBs are associated with weight gain. Te Morenga et al. intended to investigate the association between free sugars intake and obesity, but remarked that most cohort studies used SSB as the free sugar measure (Te Morenga et al. 2013). Large population-based studies in adults providing evidence that sugar intake per se would be associated with obesity are indeed scarce.

Findings from cross-sectional studies have suggested that high consumers of added sugars, NMES, or sucrose weigh less and have lower BMI than moderate consumers (Lewis et al. 1992, Gibson 1996, Drewnowski et al. 1997). An inverse association between sugar intake expressed as E% and obesity has also been reported to be sex-specific, with an association in men, but not in women (Macdiarmid et al. 1998). In the Scottish Heart Health and MONICA Studies, including 11 626 adults, from the lowest to the highest fifth of extrinsic sugar intake (E%), a 4-fold (18% to 4.4%) and nearly 2-fold (23% to 13%) decline in obesity prevalence was evident in men and women, respectively (Bolton-Smith and Woodward 1994). A more recent study in New Zealand adults reported that the inverse association was evident for total sugars, but not for sucrose (Parnell et al. 2008).

The few identified prospective studies in this study area (Table 8) did not find an association between sucrose intake and weight change (Colditz et al. 1990, Parker et al. 1997). An exception was reported in a recent sucrose intake biomarker study including 1734 adults participating in the EPIC-Norfolk Study in the UK (Kuhnle et al. 2015). In this study, energy-adjusted sucrose intake, based on 7-day FR, was associated with a decreased likelihood of being overweight or obese after a 3-year follow-up (odds ratio (OR): 0.56; 95% CI: 0.40-0.77 for highest vs. lowest quintile). The corresponding OR (95% CI) based on the predictive sucrose intake biomarker measured from spot urine samples at baseline was 1.54 (1.12-2.12).

Taken together, the putative role of sugar intake in obesity development is not clear in light of prospective cohort studies and further research is needed. Cultural differences, the non-uniform definitions of sugars, and the possible confounding factors associated with food sources of sugar may explain some of the inconsistency. In addition, shortcomings of the self-report dietary assessment methods, such as misreporting of sugar-containing foods, especially in obese individuals warrant consideration. Also reverse causation, i.e. obese individuals decreasing their intake of sugar-rich foods, is one likely explanation for inverse associations between sugar intake and obesity found in some studies.

Dietary fibre

Several prospective studies have investigated the role of fibre in obesity development (Table 8). Early analysis in the NHS (n=31 940) (Colditz et al. 1990) and the Danish arm of the MONICA Study (n=1762) (Iqbal et al. 2006) did not yield associations between fibre intake and weight change in 4-year and 5-year follow-ups, respectively. In contrast, both the CARDIA Study (Ludwig et al. 1999) and the EPIC study (Du et al. 2010) have demonstrated significant inverse associations between total fibre intake and weight change. In the EPIC Study, the association between fibre intake and obesity during a 6.5-year follow-up was affected by fibre source. A daily increase of 10 g of cereal fibre was associated with a 77 g/year decrement in weight and a 0.10 cm/year decrement in WC. However, fruit and vegetable fibre were inversely associated with WC only (Du et al. 2010). Low fibre intake has also been associated with increased visceral adiposity in 48 631 subjects participating in the EPIC Study (Romaguera et al. 2010). A smaller study with body composition measurement (BodPod chamber) and a 20-month follow-up in American adults found that fibre intake was inversely associated with body fat percentage (Tucker and Thomas 2009). Further evidence of an inverse relationship between fibre intake and obesity were the findings of the NHS and the Health Professionals Follow-up Study (HPFS), with 12-year and 9-year follow-up times, respectively (Liu et al. 2003, Koh-Banerjee et al. 2003). Liu et al. reported that women with the greatest increase in fibre intake gained 1.52 kg less weight (P for trend <0.0001) and were 49% less likely to gain weight than women with the smallest increase (OR (95% CI): 0.51 (0.39-0.67) for highest vs. lowest quintile). In male health professionals, a 12 g increase in fibre intake was associated with a 0.63 cm decrease in WC (Koh-Banerjee et al. 2003). In summary, cohort studies point towards the protective role of fibre in relation to obesity, which has strong evidence also from controlled trials (Slavin 2005, Scientific Advisory Committee on Nutrition 2015). However, the specific role of different food sources of fibre (different fibre types) should be investigated further from the epidemiological perspective (Stephen et al. 2017).

Dietary GI and GL

The cross-sectional findings regarding the effect of dietary GI and GL on obesity outcomes in the general adult population have been conflicting. The Danish Inter99 Study found a positive association between GI and GL and BMI both in the entire

population (n=6334) and when low energy reporters were excluded and adjustments were made for energy (Lau et al. 2005). Similarly, positive associations between GI and GL and both general and abdominal obesity emerged in the 1487 participants of the UK NDNS (Murakami et al. 2013). In contrast, in the smaller IRAS Study, with 30% of subjects having impaired glucose tolerance, GI was not associated with BMI or WC. In this study, the positive association between GL and obesity measures was explained by total energy intake (Liese et al. 2005). Two studies with approximately 8000 adult subjects from Mediterranean countries have reported either no association (Rossi et al. 2010), or an inverse association for GL (Mendez et al. 2009) when investigating BMI as an outcome in an energy-adjusted model. Finally, the Cooper Center Longitudinal Study from USA reported a positive association between GI and WC in both sexes, whereas GL was inversely associated with WC in men, but not in women (Finley et al. 2010).

The prospective cohort studies also provide mixed findings (Table 8). Two rather small prospective studies with fewer than 600 subjects and follow-up times of 1 and 6 years, respectively, did not find associations between GL and obesity measures (Ma et al. 2005, Hare-Bruun et al. 2006). While Ma et al. reported a positive association between GI and BMI in the entire cohort, Hare-Bruun et al. saw this result only in women, especially in sedentary women. A Spanish study with a 5-year follow-up was unable to demonstrate any associations between GI or GL and obesity measures after adjusting for multiple confounders (de la Fuente-Arrillaga et al. 2014). The two largest prospective studies were conducted in the EPIC Study (Du et al. 2009a, Romaguera et al. 2010). In a 6.5-year follow-up of 89 000+ Europeans, no association between GI and GL and weight change could be demonstrated, but GI was positively associated with WC in both sexes (Du et al. 2009a). With every 10-unit higher GI, WC increased by 0.19 cm per year (Du et al. 2009a). Later, these findings were supported by a positive association between GI and visceral adiposity (Romaguera et al. 2010). This study reported also that GL was associated with visceral adiposity in a 5.5-year follow-up in women, but not in men.

To summarize, prospective cohort studies provide a mixed picture on the effect of GI and GL in relation to obesity outcomes. Apparently, there might be both population-related and methodological explanations. The latter include the GI database-related challenges, the utilization of different obesity measures, and analytical choices related to the modelling of the GI/GL-obesity relationship. As noted earlier, dietary GI most probably is a marker of other dietary dimensions (Schulz et al. 2005), which deserves consideration in epidemiological research on dietary GI and GL.

Table 8. Prospective cohort studies on the relationship between carbohydrate factors and obesity outcomes in general adult populations.

Reference	Country, Study	Population	Follow-up	Diet method	Exposure	Outcome	Adjustments	Results
Colditz et al. 1990	USA, Nurses' Health Study	31940, 30-55 years, w	4 years	FFQ	Total carbohydrate, sucrose, fibre, g/day	weight change (self-reported)	age, baseline weight, energy intake	Total carbohydrate: ↓ Sucrose: NS Fibre: NS
Haffner et al. 1991	USA, San Antonio Heart study	2217, 25-64 years, m+w	8 years	Dietary recall	Total carbohydrate, g/day and E%, sucrose and starch, g/day	weight change (measured)	age	Total carbohydrate: NS Sucrose: NS Starch: NS
Rissanen et al. 1991	Finland, Mobile Clinic Health Survey	12669, 30-64 years, m+w	5.7 years	Dietary history	Total carbohydrate, E%	weight change (measured)	age	Total carbohydrate: ↑ (women only)
Parker et al. 1997	USA, Pawtucket Heart Health Program	465, 18-64 years, m+w	4 years	FFQ	Total carbohydrate, sucrose, and sweets, g/day	weight change (measured)	age, energy intake, BMI, physical activity, smoking	Total carbohydrate: NS Sucrose: NS Sweets: NS
Ludwig et al. 1999	USA, CARDIA Study	2909, 18-30 years, m+w	10 years	FFQ	Total carbohydrate E% and fibre, E%	weight change and WHR change (measured)	age, gender, alcohol, weight, centre, education, energy intake, physical activity, smoking	Body weight: Total carbohydrate: ↓ Fibre: ↓ WHR: Total carbohydrate: NS Fibre: ↓
Koh-Banerjee et al. 2003	USA, Health Professional's Follow-up Study	16587, 40-75 years, m	9 years	FFQ	Fibre, g/day	WC change (self-reported)	age, BMI, waist, smoking, physical activity, dietary changes, energy intake, fat, protein, alcohol	Fibre: ↓

Table 8 (continued)

Reference	Country, Study	Population	Follow-up	Diet method	Exposure	Outcome	Adjustments	Results
Liu et al. 2003	USA, Nurses' Health Study	74091, 38-63 years, w	12 years	FFQ	Fibre, g/day	weight change (self-reported)	age, baseline weight, changes in covariate status (physical activity, smoking and dietary factors)	Fibre: ↓
Ma et al. 2005	USA	572, 20-70 years, m+w	1 year	7-day FR	Total carbohydrate, g/day and E%, dietary GI and dietary GL	BMI (measured)	age, sex, race, education, employment, smoking, baseline BMI, physical activity, energy intake	Total carbohydrate: NS GI: ↑ GL: NS
Iqbal 2006	Denmark, MONICA Study	1762, 30-60 years, m+w	5 years	7-day FR	Total carbohydrate, E% and fibre, g/day	weight change (measured)	age, education, BMI, cohort, physical activity, smoking, energy intake, food volume	Total carbohydrate: NS Fibre: NS
Hare-Bruun et al. 2006	Denmark, MONICA Study	376, 35-65 years, m+w	6 years	Dietary history interview	Dietary GI and GL	weight change, change in body fat %, WC change (measured)	baseline outcome variable, age, smoking, education, physical activity, energy intake, protein, fat, and fibre	<i>Weight, body fat%, WC:</i> GI: ↑ (women only, especially sedentary women). GL: NS (both sexes)
Halkjaer et al 2006	Denmark, Danish Diet Cancer and Health Study	42696, 50-64 years, m+w	5 years	FFQ	Total carbohydrate from different food sources, g/day	WC change (self-reported)	age, physical activity, smoking, alcohol, and energy intake	Total carbohydrate: NS Carbohydrates from refined grains and potatoes and food with simple sugars: ↑ Carbohydrates from fruits and vegetables: ↓ (women only).
Tucker & Thomas 2009	USA	252, avg 40 years, w	20 months	7-day weighed FR	Total fibre, soluble fibre, and insoluble fibre, g/1000 kcal	weight change, change in body fat % (measured)	age, physical activity, season, time between measurements, energy intake	<i>Weight and body fat%:</i> Total fibre: ↓ Soluble fibre: NS (borderline) Insoluble fibre: NS (borderline)

Table 8 (continued)

Reference	Country, Study	Population	Follow-up	Diet method	Exposure	Outcome	Adjustments	Results
Du et al. 2009	Europe, EPIC	89432, 20-78 years, m+w	6.5 years	FFQ	Dietary GI and GL	weight change and WC change (partly self-reported)	age, sex, anthropometrics, smoking, physical activity, education, follow-up duration, nutritional factors, menopausal status (w)	<i>Weight:</i> GI: NS GL: NS <i>WC:</i> GI: ↑ GL: NS
Du et al. 2010	Europe, EPIC	89432, 20-78 years, m+w	6.5 years	FFQ	Total fibre, cereal fibre, and fruit and vegetable fibre, g/day	weight change and WC change (partly self-reported)	see Du et al. 2009	<i>Weight:</i> Total fibre and cereal fibre: ↓ Fruit and vegetable fibre: NS <i>WC:</i> Total fibre and cereal fibre: ↓ Fruit and vegetable fibre ↓
Romaguera et al. 2010	Europe, EPIC	48631, avg 50 years, m+w	5.5 years	FFQ	Total carbohydrate, E%, fibre, g/day; dietary GI and GL	change in visceral adiposity (WC adjusted for BMI)	age, sex, physical activity, education, nutritional factors, menopausal status (w)	Total carbohydrate: NS GI: ↑ (both sexes) GL: ↑ (women only) Fibre: ↓ (women only)
de la Fuente-Arrillaga et al. 2014	Spain, Seguramiento University of Navarra Study	9267	5 years	FFQ	Dietary GI and GL	weight change, BMI (self-reported)	age, sex, baseline BMI, smoking, physical activity, sedentary behaviours, fibre, energy intake, nutritional factors	GI: NS GL: NS
Kuhnlé et al. 2015	UK, EPIC-Norfolk	1734, 39-77 years, m+w	3 years	7-day FR, and sucrose intake biomarker	Sucrose, E%, sucrose concentration adjusted by specific gravity	BMI (measured)	age, sex, energy intake	Self-reported sucrose intake (E%): ↓ Biomarker-based sucrose intake: ↑

FFQ, food frequency questionnaire; FR, food records; m, men; w, women; GI, glycaemic index; GL, glycaemic load; BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; Associations: ↑=positive, ↓=negative, NS=non-significant; CARDIA, Coronary Artery Risk Development in Young Adults; MONICA, Multinational Monitoring of trends and determinants in Cardiovascular Disease; EPIC, European Prospective Investigation into Cancer and Nutrition Study.

2.5 SUMMARY OF THE LITERATURE REVIEW

Overall, food intake of modern populations is shaped by a changing food environment characterized by a high supply of processed foods. This is likely to cause changes in the intake of carbohydrate-containing foods and dietary composition, thereby potentially impacting long-term public health.

Dietary assessment of nutritional epidemiological studies relies on food composition information maintained in FCDBs as well as dietary self-report instruments such as FFQs. These methodological starting points warrant consideration when the relationship between dietary carbohydrates and health outcomes is investigated. Regarding GI, the compilation process of GI datasets for epidemiological research purposes appears similar across the literature. However, this process relies on subjective decisions of the dataset compilers. Thus, the transparency of GI-related information should be improved in FCDBs to facilitate comparability of information and evaluation of data quality. Documentation of GI values with controlled vocabularies of a standardized FCDB framework has thus far not been described. Regarding dietary intake assessment instruments, large variation appears to exist in the relative validity of comprehensive FFQs in measuring dietary carbohydrates across populations. Overall, FFQ validation studies concentrating on dietary carbohydrates are scarce. Due to culture- and time-specificity of FFQs, validation studies should be regularly conducted to improve interpretation of nutritional epidemiological studies.

The changing food environment challenges understanding on the relationship between dietary carbohydrates and health. The role of added sugars in the total dietary context needs clarification. The view that added sugars affect the diet negatively (e.g. nutrient dilution) is supported by studies showing an association between added sugars and low dietary fibre intake and low fruit and vegetable consumption. However, the associations between added sugars and other dietary components are insufficiently documented in modern adult populations and should be further examined. Due to the generally high prevalence rate of obesity and its central role as a risk factor for chronic diseases, obesity prevention remains a goal of the public health agenda. In light of the literature, dietary fibre intake appears to be consistently associated with a decreased risk of obesity. In contrast, findings on the relationship between dietary GI and GL and obesity are conflicting. Moreover, studies concerning the association between sugar intake, beyond SSBs, and obesity are scarce. Further investigations of this topic are warranted.

3 AIMS OF THE STUDY

The main aim of this thesis was to examine carbohydrate factors in relation to overall diet and obesity risk in the general adult population. Both food composition data description and the relative validity of the dietary intake assessment instrument were covered.

Specific aims of Studies I-IV were as follows:

1. To determine whether the controlled vocabularies used in the Finnish national food composition database are suitable for GI (I).
2. To examine the relative validity of the FFQ in measuring carbohydrate factors (i.e. total carbohydrate, starch, total sugars, fructose, lactose, sucrose, dietary fibre, insoluble dietary fibre, soluble polysaccharides, dietary GI and GL) (II).
3. To assess whether subject's age, education, and BMI are associated with the between-method agreement in the FFQs and FRs when measuring carbohydrate factors (see point 2 for definition of carbohydrate factors) (II).
4. To evaluate associations between added sugars (i.e. intake estimate based on sucrose and fructose), macronutrient intake, and food consumption (III).
5. To determine whether carbohydrate factors (i.e. total carbohydrate, sucrose, lactose, dietary fibre, dietary GI and GL) are associated with obesity risk in a pooled analysis of three cross-sectional population-based studies (IV).

4 METHODS

4.1 STUDY POPULATIONS

This thesis is based on four population-based health examination surveys of Finnish adults conducted at the National Institute for Health and Welfare (THL) during 2000-2007 (Table 9).

4.1.1 DIETARY LIFESTYLE AND GENETIC DETERMINANTS OF OBESITY AND THE METABOLIC SYNDROME STUDY (I-IV)

The Dietary Lifestyle and Genetic determinants of Obesity and the Metabolic syndrome (DILGOM) Study aims at identifying factors associated with obesity from a multidisciplinary perspective. The DILGOM Study subjects originally participated in the National FINRISK 2007 Study, a cross-sectional population-based health survey. The FINRISK studies have been conducted at 5-year intervals since 1972 to monitor chronic disease risk factors in Finland (Borodulin et al. 2015). FINRISK 2007 subjects were a random sample of 10 000 individuals aged 25-74 years drawn from the Finnish Population Information System. The sample was stratified according to sex, 10-year age group, and five large geographical areas (capital area, South-western Finland, North Karelia, Northern Savo, and Ostrobothnia). The subjects received via mail an invitation letter to a health examination, and a self-administered health questionnaire. The health examinations were carried out in January-March 2007. All FINRISK 2007 subjects (n=6258 response rate 63%) were invited to the DILGOM Study, conducted in April-June 2007 (Kontinen et al. 2010). Of those invited, 5024 (80%) participated and underwent a health examination. In addition, subjects filled in detailed health questionnaires, including an FFQ.

4.1.2 NATIONAL FINDIET 2007 SURVEY (I, II)

The National FINDIET 2007 Survey (FINDIET 2007), examining the food consumption and dietary intake of adult Finns, comprised a randomized sub-sample (33%) of the FINRISK 2007 Study (Reinivuo et al. 2010). Of these 3286 subjects, 2054 subjects completed a 48-hour dietary recall (48-hour DR, two times a 24-hour DR concerning consecutive days) during the FINRISK health examination (62.5% of those invited). In addition, half of the original FINDIET sample was stratified to the diet recording sub-sample (n=1646). Of these, 1039 subjects were instructed to fill in two 3-day food records (FR) after the 48-hour DR. A total of 914 subjects completed the first FR in January-March 2007, whereas 624 subjects returned the second FR in June-October 2007.

4.1.3 HELSINKI BIRTH COHORT STUDY (I, IV)

The Helsinki Birth Cohort Study (HBCS) includes two historical birth cohorts comprising individuals born in Helsinki University Central Hospital during 1924-1933 and 1934-1944. This thesis utilizes data from the second cohort containing 8760 men and women. In the year 2000, these cohort members were traced by using unique identification numbers of the Finnish Population Information System and sent a health questionnaire (n=7078). In total, 4515 (64%) responded. Of these participants, a sample of 2902 individuals residing in the Helsinki metropolitan area was derived using random number tables and invited to a clinical examination conducted in 2001-2004 (Ylihärsilä et al. 2008). Eventually, 2003 individuals underwent the health examination (response rate 69%) and filled in the health questionnaires.

4.1.4 HEALTH 2000 HEALTH EXAMINATION SURVEY (I, IV)

The Health 2000 Health Examination Survey (Health 2000) aimed at assessing the major public health challenges, their causes and treatment as well as the health status, functional capacity, and working ability of Finnish residents aged ≥ 30 years (Heistaro 2008). The survey was conducted during 2000-2001 and involved a nationally representative sample of 8028 individuals drawn from the Finnish Population Information System. The sampling followed a stratified two-stage clustering design. First, 80 health care districts out of the total of 249 districts in mainland Finland were selected, and second, a random sample within the districts was drawn. Subjects received via mail an invitation letter to a health interview conducted in their home. All those who participated in the interview (n=6986, response rate 87%) were scheduled an appointment for a health examination. The participation rate in the health examination was 84% (n=6772). The subjects were also provided with health questionnaires.

4.2 ETHICAL APPROVAL

The FINRISK 2007 (including FINDIET 2007) Study, the DILGOM Study, the HBCS, and the Health 2000 Survey were conducted according to the guidelines laid down in the Declaration of Helsinki. All procedures involving human subjects were approved by the Ethics Committee of the Hospital District of Helsinki and Uusimaa. Written informed consent was obtained from all subjects prior to commencement of the study.

Table 9. General characteristics of survey data included in the four studies of the thesis.

Characteristic	DILGOM ¹	FINDIET 2007 ¹	HBCS	Health 2000
Included in studies	I-IV	I, II	I, IV	I, IV
Year of data collection	2007	2007	2001-2004	2000-2001
Age range	25-74	25-74	56-70	≥ 30
Invited ²	6258	3286	2902	6986
Participated ³	5024 ⁴	2069	2003 ⁴	6772 ⁴
<i>Dietary data</i>				
Returned FFQ	4996	-	2003	6373
Provided 48-hour DR	-	2054	-	
Returned 2*3-day FR	-	624	-	

DILGOM, Dietary, Lifestyle, and Genetic determinants of Obesity and the Metabolic syndrome Study; FINDIET 2007, The National FINDIET 2007 Survey; HBCS, Helsinki Birth Cohort Study; Health 2000, The Health 2000 Health Examination Survey; FFQ, food frequency questionnaire; DR, dietary recall; FR, food record.

¹ Part of FINRISK 2007 Study.

² Number of subjects originally invited to the health examination.

³ Number of subjects who underwent the health examination. In case of FINDIET 2007 this refers to the FINRISK 2007 health examination.

⁴ Subjects provided with a FFQ.

4.3 DIETARY INTAKE ASSESSMENT

4.3.1 FOOD FREQUENCY QUESTIONNAIRE (I-IV)

The habitual diet of subjects participating in health examinations (DILGOM, Health 2000, and HBCS) was assessed using a comprehensive semi-quantitative food frequency questionnaire (FFQ). The FFQ was originally developed and validated as part of the Kuopio Breast Cancer Study (Männistö et al. 1996), thereafter further developed and repeatedly updated for use in the Finnish general population. Health 2000 and HBCS utilized the version described by Paalanen (Paalanen et al. 2006), whereas the DILGOM study utilized the version described in this thesis (II). The different FFQ versions did not differ substantially from each other.

The FFQ inquired into the average consumption of 128-131 food items during the previous year (last 12 months). In the FFQ, the items were grouped into 12 food group entities (Table 10). In addition, beneath each entity there was a space in which subjects could report additional, frequently consumed foods not listed in the questionnaire. The FFQ included nine possible frequency categories for all of the FFQ items, ranging from never or seldom to six or more times per day. The portion size for each food item and mixed dish appeared on the FFQ as household or natural units (e.g. glass or slice) or as ‘portion’. These portion sizes were based on the 48-

hour DR data of FINDIET 2007 (Reinivuo et al. 2010) and determined separately for men and women (DILGOM and HBCS). In Health 2000, identical portion sizes for both sexes were used. These were based on the FINDIET 1997 data (Anttolainen et al. 1998). In addition to portion size determination, the FINDIET Surveys were used to update the contents of the FFQs to better reflect the current selection of foods on the market and the most popular dishes consumed by Finnish adults. These updates concerned both the FFQ food items and the food code selection for each item (Table 10). Each FFQ item was composed of 1-8 of the most consumed foods or dishes within the given food use group. These food codes established the link between the FFQ item and the food composition database (see Sections 4.3.4 and 4.3.5).

In the DILGOM Study and HBCS, the subjects completed the FFQ on paper at the study site where trained research staff reviewed its completeness. In the Health 2000 Survey, the FFQ was provided after the health examination on paper, and the subjects were advised to complete it at home and mail it to THL for data entry.

In this thesis, FFQ data was used in all four studies (I-IV). GI values were determined for all foods encoded in the different FFQ versions (I). In Studies II-IV, the FFQ method also enabled dietary intake assessment.

Table 10. *Summary of food frequency questionnaire contents.*

Food group entity		FFQ food items ¹		Food codes ²	
#	Food group	2006 ³	2012 ⁴	2006 ³	2012 ⁴
1	Milk products	12	12	31	34
2	Cereal products	16	16	54	66
3	Fat spreads	4	4	9	11
4	Vegetables and vegetable dishes	22	22	59	69
5	Potato, pasta, and rice	6	6	17	24
6	Meat and meat dishes	18	18	58	63
7	Fish and fish dishes	9	9	23	27
8	Poultry dishes and eggs	3	3	9	10
9	Fruit and berries	7	8	21	23
10	Desserts	4	5	7	12
11	Confectionary and snacks	7	6	16	19
12	Beverages	21	22	31	39
<i>Total</i>		128	131	335	397

¹ Number of food items appearing on the FFQ

² Number of food codes of the Fineli FCDB (Reinivuo et al. 2010) used to compose the FFQ items

³ FFQ version used in Health 2000 and HBCS (Paalanen et al. 2006)

⁴ FFQ version used in DILGOM (Study II)

4.3.2 48-HOUR DIETARY RECALL (I)

At the FINDIET 2007 study sites, trained nutritionists carried out computer-assisted face-to-face dietary recall interviews concerning the two previous days (48-hour DR) (Paturi et al. 2008). The protocol featured two steps: a chronological review of eating occasions (nature of occasion, time, location) and a detailed recall of all consumed foods and beverages. The in-house Finessi software was used to enter the data, including immediate coding of foods and beverages with codes of the Finnish national food composition database (Reinivuo et al. 2010). To assist the subjects in their recall, package photographs of the most common margarine, yoghurt, and juice were available. For estimation of portion sizes, a validated and tested picture book (Paturi et al. 2006, Ovaskainen et al. 2008) was utilized.

In this thesis, the 48-hour DR was used to identify foods currently consumed by the adult population in Finland. This formed the basis for both FFQ updates (items, food codes, and portion sizes) and contributed to the food list for which GI values were determined (I).

4.3.3 FOOD RECORDS (I, II)

Subjects belonging to the FINDIET 2007 diet-recording sub-sample were asked to fill in two 3-day FR in order to capture longer term dietary intake and seasonal variation in diet (Paturi et al. 2008). The first 3-day FR period started from the day following the 48-hour DR (Jan-March 2007). The second 3-day FR was mailed to those subjects who had returned their first FR to THL (June-October 2007). In the food-recording protocol, subjects were instructed to detail the time, eating occasion type, and location as well as the types and amounts of all foods and beverages consumed during the 3-day period. Subjects were encouraged to immediately record consumption during the eating occasion to avoid memory lapses. Moreover, subjects were discouraged from changing their dietary habits during recording. Portion size estimation was based on household measures, standard portion sizes of packaged foods, and the same picture book that was used in the 48-hour DR (Paturi et al. 2006). All FRs and the picture books were returned to THL by mail, and thereafter, nutritionists entered the data using uniform coding decisions.

The two 3-day FRs of the FINDIET 2007 formed the reference method for the validation of the FFQ (II). All foods identified with FRs required GI values (I).

4.3.4 FOOD COMPOSITION DATABASE

Finnish national food composition database

The nutritional assessment of this thesis relied on the Finnish national food composition database Fineli[®] (Reinivuo et al. 2010). In general, Fineli comprises approximately 1500 basic ingredients and 2500 composite foods and dishes (foods prepared at home or processed by the food industry and catering services). The content of Fineli is updated constantly with analysed values mainly based on Finnish

studies, adopted values from food the food industry, and international, mainly Nordic food composition tables and databases. The standard recipes of composite foods are based on the best-selling Finnish cookbooks and popular Internet recipe archives.

Assigning GI values for Finnish foods (I)

Due to the lack of GI values in the Fineli database, a comprehensive list of Finnish foods was desired in order to create a GI database. Foods contained in the FFQ, 48-hour DR, and the two 3-day FR formed the food list.

The GI values were based on the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study GI database (Similä et al. 2009). Moreover, the identified food list contained new foods not found in the ATBC Study GI database. In general, GI values were obtained from sources where GI measurement methodology could be verified to adhere to international recommendations (WHO 1998, Brouns et al. 2005). A total of four minimum quality criteria were applied when selecting the values: 1) glucose or white bread were used as the reference, 2) test and reference food contained a similar amount of glycaemic carbohydrate (50 g or 25 g), 3) study subjects were not insulin-treated, and 4) the testing included ≥ 6 subjects (Similä et al. 2009). Data sources for GI values included peer-reviewed scientific journals, among them values of the THL laboratory (Hätönen et al. 2006). In addition, unpublished analytical values for typical Finnish foods from the THL laboratory were used. Unpublished values were also derived from the International Tables of Glycaemic Index and Glycaemic Load Values (Atkinson et al. 2008).

All GI values were assigned relative to the glucose standard, i.e. the GI of glucose solution = 100. GI values measured relative to the white bread standard were converted to the glucose standard by multiplying the values by a factor of 0.7 (WHO 1998). GI was set to zero, when the food contained no carbohydrate (e.g. plain meat, oils) or only negligible amounts of carbohydrate, thereby contributing only minutely to the dietary carbohydrate supply (e.g. some low-fat margarines, liver). An arithmetic mean of values was applied in case of several available values for a given food. For missing values, the GI of a related food was imputed (e.g. the most similar food in terms of food structure and carbohydrate source).

Value documentation

The Fineli database follows the European food data standard (Finnish Standards Association 2013) and utilizes controlled vocabularies established within the European Food Information Resource (EuroFIR) Network in value documentation (Møller et al. 2008). The core controlled vocabularies of EuroFIR were applied for the first time for GI values in this thesis (I). In the Fineli database, the same vocabularies are used in the description of all dietary factors. Therefore, we also assessed the origin of values (description terms included in the Acquisition type thesaurus) and the derivation methods of the values (description terms included in the Method type thesaurus) for carbohydrate, starch, dietary fibre, lactose, sucrose, and fructose. This assessment covered foods encoded in the FFQ (number of food codes=397).

4.3.5 CALCULATION PROCEDURES

Dietary data (FFQ, 48-hour DR, and two 3-day FR) were converted into daily intakes of nutrients and food groups, dietary GI and GL, by linking them to the Fineli database through calculation software developed at THL (Finessi). The calculation procedures related to composite foods followed international recommendations (Reinivuo et al. 2009). In this thesis, food groups were mainly defined as groups having a common origin in a particular foodstuff (e.g. wheat, potato), i.e. ingredient class or foods derived through decomposition of composite foods. In the FR, the daily average weights of the consumed foods were obtained as an arithmetic mean of the given food entries (II). In the FFQ, daily weights of FFQ items were obtained by multiplying the indicated frequencies of consumption by the fixed portion sizes (II-IV).

Composite food GI values (I-IV)

The composite food GI was calculated through 1) deriving GI values and carbohydrate contents of all food ingredients, 2) calculating the proportional contribution of each ingredient to composite food carbohydrate content, 3) multiplying the proportional carbohydrate content of each ingredient with the corresponding ingredient GI value to yield proportional GI values, and 4) summing up the proportional GI values (WHO 1998). If all composite food ingredients had a GI value of zero, the GI of the composite food resulted in a zero value (for equation and an example, see Appendix 1).

Dietary GI and GL (II, IV)

For both the FFQ and the FR, dietary GI values were calculated as the weighted mean of the GI values of all carbohydrate-containing foods in the diet. In the weighting the proportion of the total carbohydrate content provided by each food was taken into account (Wolever et al. 1991, Wolever et al. 1994). Dietary GL was calculated by multiplying the dietary GI value with the carbohydrate content of the diet and dividing by 100 (Salmerón et al. 1997) (for equations, see Appendix 1).

Naturally occurring and added sugars (III)

In Study III, the perspective to dietary sugars was restricted to the disaccharide sucrose and the monosaccharide fructose. Sucrose is the main sweetener used in households and the food industry and has been applied as a proxy measure of added sugar in the national FINDIET Surveys (Paturi et al. 2008, Helldán et al. 2013).

Due to the lack of separate values for naturally occurring sucrose or fructose and added sucrose or fructose in the Fineli database, the composite food disaggregation procedure was applied to yield sucrose and fructose values at a basic ingredient level. All sucrose and fructose from the ingredient groups fruits, berries, 100% fruit juice, and vegetables were summed to yield the naturally occurring sugars variable. The variable ‘added sugars’ was formed by subtracting naturally occurring sucrose and fructose from total sucrose and fructose.

4.4 CLINICAL EXAMINATIONS

During the health examinations trained research nurses measured height, weight, and waist circumference of the subjects according to international standardized protocols (Tolonen et al. 2008). Height was measured to the nearest 0.1 cm (except in Health 2000 to the nearest 0.5 cm) and weight to the nearest 0.1 kg. A soft measuring tape was used to measure waist circumference at the midpoint between the lowest rib and iliac crest. Body mass index (BMI, kg/m^2) was computed as weight (kg) divided by squared height (m). Obesity was defined as $\text{BMI} \geq 30 \text{ kg/m}^2$ for both sexes and elevated waist circumference as $\text{WC} \geq 102 \text{ cm}$ for men and $\text{WC} \geq 88 \text{ cm}$ for women (WHO 2000, WHO 2008).

4.5 ASSESSMENT OF BACKGROUND VARIABLES

Health questionnaires inquiring about subjects' education, leisure-time physical activity, and smoking status were administered during the health examination. In Studies II and III, the total number of education years was used to classify subjects into three educational levels (low, middle, and high) according to birth year. This accounted for the increase of average school years and the extension of the basic education system over time. In Study IV, total years of schooling were used, since this variable was identified as common for DILGOM, HBCS, and Health 2000.

In Study III, leisure-time physical activity was computed as a 3-level categorical variable: inactive (mainly light activities, e.g. reading, watching television), moderately active (e.g. walking, cycling, or gardening at least 4 hours per week), active (physically demanding activities, e.g. running, cross-country skiing, or swimming at least 3 hours per week). In Study IV, leisure-time physical activity included three categories (mild shortness of breath and perspiration <1 time/wk, 1-3 times/wk, ≥ 4 times/wk), since this variable was identified as common for DILGOM, HBCS, and Health 2000.

Smoking status was defined by using three categories: never-smoker, quit, and current smoker (III and IV).

4.6 STUDY DESIGNS

In Study I, the process of assigning GI values to an existing food composition database framework was described, and assessed from the view-point of value documentation. Studies II-IV were observational in nature. In the FFQ validation study (II), the administration sequence of the test method (FFQ) and the reference method (two 3-day FR) was alternating. The two FR periods were timed approximately 6 months apart (January-March 2007 and June-October 2007). The FFQ was administered in-between the FR periods (Figure 4). The designs of Studies III and IV were cross-sectional.

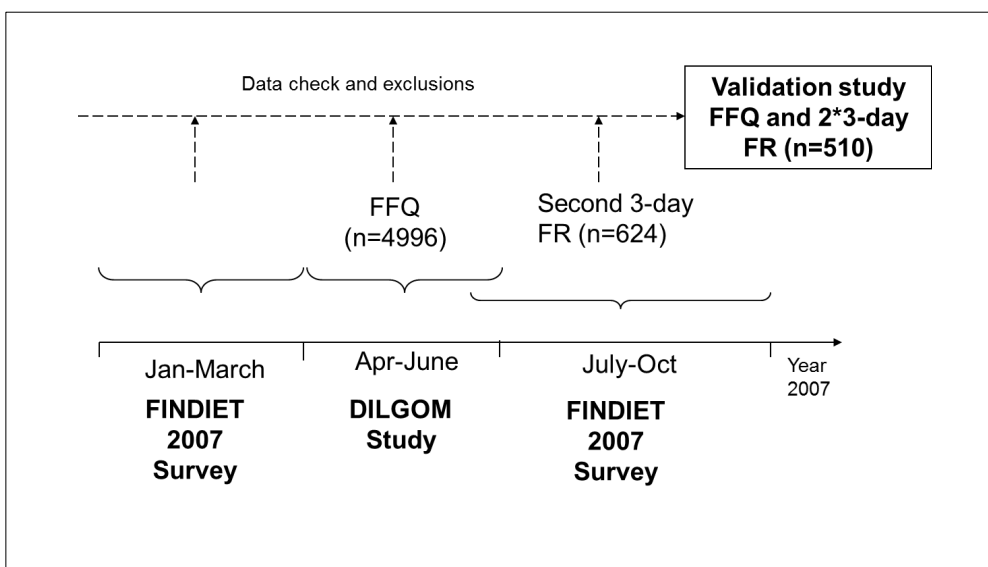


Figure 4 Administration sequence of test method (FFQ, food frequency questionnaire) and reference method (FR, food record) in the validation study (Study II).

4.7 EXCLUSION CRITERIA

The food list in Study I included foods identified from acceptable 48-hour DR and FR (n=2048 different foods after exclusion of duplicates). Due to overlapping foods, the foods encoded in the FFQ versions produced an additional 162 foods. In all, the final food list requiring GI values covered 2210 foods.

The FFQ validation study (II) included subjects who completed two 3-day FRs. Of such 624 subjects, 18 were excluded due to incomplete recording, and 45 did not return or provide an acceptable FFQ. Further exclusions were made due to FR classified as unreliable during the data entry (n=45) and diet-affecting illness (e.g. stomach flu) during recording (n=6), resulting in 510 eligible subjects (218 men and 292 women).

Overall, Studies II-IV were based on subjects who had completed the FFQ. In all studies, exclusions were made due to missing FFQ, incompletely filled FFQ, and daily energy intake cut-offs corresponding to 0.5% at both ends of sex-specific daily energy intake distributions (DILGOM and HBCS) or daily energy intake values < 600 and > 7000 kcal/d (Health 2000) (Meltzer et al. 2008). This was done to eliminate subjects with implausible usual energy intakes. Moreover, in Studies III and IV, pregnant women were excluded, as were subjects with missing BMI. In Study IV, exclusions were also made due to old age (>79 years). A summary of the exclusions and final sizes of analytical data for Studies II-IV is provided in Figure 5.

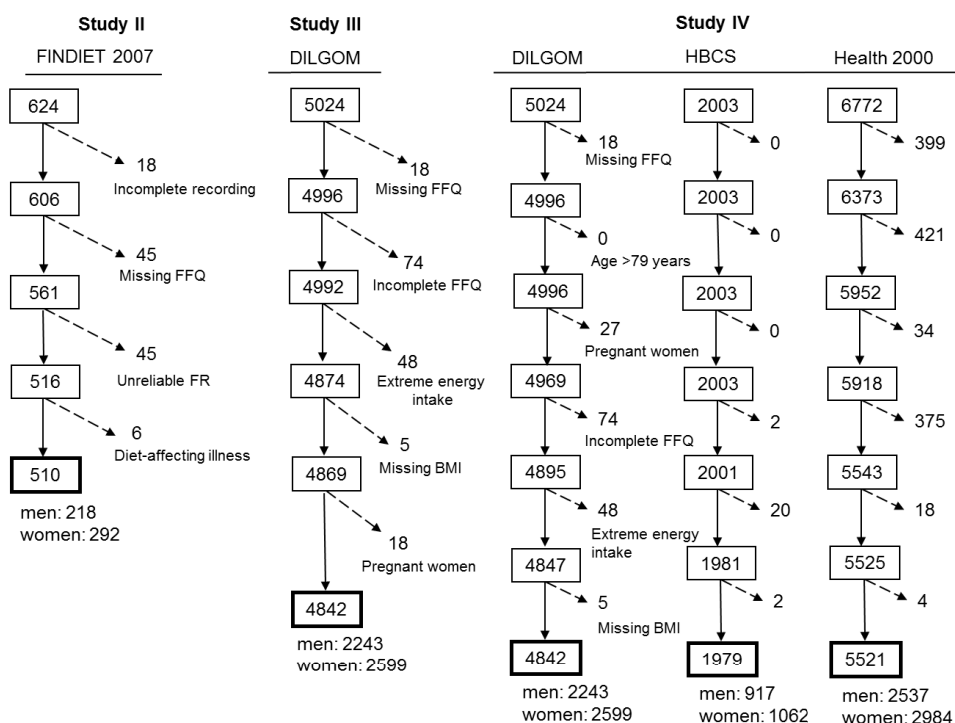


Figure 5 Exclusion criteria and final population sizes of Studies II-IV.

4.8 STATISTICAL METHODS

All analyses were performed using the SAS statistical software package (SAS Institute Inc., Cary, NC, USA). Study II was performed with version 8.2, Study III with version 9.3, and Study IV with version 9.2. Study I did not require statistical analysis.

4.8.1 COMMON STATISTICAL METHODS (II-IV)

Nutrient intakes and dietary GI and GL were log (natural)-transformed in order to satisfy the normality assumption and subsequently adjusted for total energy intake by using the residual method (Willett and Stampfer 1986). In addition, food group variables were log (natural)-transformed prior to analysis. In Studies II and III, the analyses were performed separately for men and women due to sex-specific portion sizes and the assumption of different general health behaviour. Sex was taken into account as both a confounder and an effect modifier in Study IV.

In Studies II-IV, background characteristics were presented as means and proportions. Standard deviations (SDs) were calculated to represent the variation in data variables. The variable trends across quartiles were tested with general linear modelling for continuous variables (quartile median values as continuous, Wald test) and Chi-square test for binary variables. The main results of Studies III and IV were confirmed by re-running the main analyses without energy under-reporters, i.e. subjects whose reported energy intake did not correspond to their physical needs based on sex and age (ratio of energy intake to basic metabolic rate (BMR) ≤ 1.14) (Black 2000, Goldberg et al. 1991, WHO 1985). In all statistical tests, a *P*-value < 0.05 was considered significant.

4.8.2 FFQ VALIDATION (II)

For FFQ and FR, the food groups contributing most to the intake of carbohydrate fractions, and dietary GL were analysed. Spearman rank-correlation coefficients between the FFQ and FR were calculated for energy-adjusted nutrients and dietary GI and GL.

Subject proportions categorized into the same or adjacent quintile and the opposite quintile (gross misclassification) by the two methods were calculated to assess the ability of the FFQ to rank subjects according to their intakes. Agreement between test and reference method was assessed by calculating the mean ratios (FFQ/FR*100) and corresponding 95% confidence intervals (CIs) of the energy-adjusted carbohydrate factors. The Bland-Altman method (Bland and Altman 1986) was applied to test whether the difference between the methods was associated with intake level, subject age, education, and BMI. In the general linear modelling, slopes significantly different from zero indicate a relationship between the intake level or subject characteristic and the measurement error in the FFQ relative to the FR.

4.8.3 SUGAR INTAKE AND OTHER DIETARY COMPONENTS (III)

The sugar variables (naturally occurring sugar, added sugar) were divided into quartiles using sex-specific cut-offs. For the food groups, the arithmetic means and 95% CIs by sugar intake quartiles were calculated. Anti-logarithms of these were taken to yield geometric means and 95% CIs for reporting. The linear trend analyses of background, nutrient intake, and food group intakes across sugar intake quartiles were adjusted for the following confounders: age, energy intake (Model 1), and further for leisure-time physical activity, smoking status, education, and BMI.

4.8.4 ASSOCIATIONS BETWEEN CARBOHYDRATE AND OBESITY (IV)

Descriptive data were calculated by BMI group, and the differences between these were analysed using the independent sample t-test for continuous variables and Chi-square test for binary background variables. The carbohydrate variables (energy-adjusted carbohydrate, sucrose, lactose, dietary fibre, dietary GI and GL) were divided into quartiles using study-specific cut-offs, and logistic regression was used to calculate study-specific odds ratios (ORs) and two-sided 95% CIs for obesity.

In the meta-analysis, the pooled OR and its 95% CI were estimated by combining the study-specific log[OR]s in a random-effects model while weighting them by the inverse of their variance (DerSimonian and Laird 1986). The Wald test of the pooled estimates determined the statistical significance of trends across quartiles. Heterogeneity of the study-specific ORs was tested using Q statistics. The squared Wald statistic provided the pooled P-value for test of interaction.

The confounding variables included in the three models were the following: sex and age (Model 1); sex, age, education, leisure-time physical activity, and smoking (Model 2); sex, age, education, leisure-time physical activity, smoking, and total energy intake (Model 3). The main analysis (Model 3) was repeated using elevated WC as the outcome variable to demonstrate repeatability of results across different obesity measures.

Possible effect modification by sex was examined. Furthermore, effect modification of the sucrose-obesity association by fruit intake was assessed. Here, subjects were categorized into low and high fruit intake groups using study-specific median intakes as cut-off points.

5 RESULTS

5.1 GI VALUES AND VALUE DOCUMENTATION (I)

A total of 2210 foods requiring a GI value were identified. For 1322 foods (60%), GI values were stored into the Fineli database (Table 11). The remaining 888 foods (40%) received their GI value through recipe calculation. In terms of the overall GI database (food n=2210), the contribution of zero values was 16%, exact matches 15%, related foods 29%, and recipe calculation 40%.

Part of the EuroFIR controlled vocabularies and their value descriptors were directly applicable for GI values: the qualitative characteristics of the values (Value type thesaurus), the origin of the values (Acquisition type thesaurus), and the methods used to derive the values (Method type thesaurus) could be documented for all stored GI values (Table 11).

Table 11. *Application of EuroFIR controlled vocabularies in documentation of glycaemic index (GI) values in the Finnish national food composition database.*

Vocabulary	Descriptor	Count	(%)¹
Value type ²	Best estimate	974	74
	Logical zero ³	348	26
Acquisition type ⁴	Created within host system ⁵	896	68
	In-house laboratory ⁶	307	23
	Published in scientific paper	105	8
	Food composition table ⁷	14	1
Method type ⁸	Imputed from other food	641	49
	Estimated ³	348	26
	Analytical result(s) ⁹	333	25

1 Refers to 1322 (100%) GI values added to the food composition database.

2 Provides a qualitative description of the value.

3 Foods containing no or negligible amounts of available carbohydrate (GI=zero).

4 Describes the origin of the value.

5 Includes values derived through arithmetic means of several contributing values, and foods assigned a GI value of zero.

6 Includes values analysed at the National Institute for Health and Welfare, Helsinki, Finland.

7 Includes unpublished GI values from the international table of GI values (Atkinson et al. 2008).

8 Provides a general indication of the method used to obtain the value.

9 Food considered similar to GI-tested food in terms of available carbohydrate type.

The origin of the literature-based values could be further described by storing the references in cases where a single GI value was directly assigned to a food on our food list. Here, the Reference type thesaurus descriptors were applied (e.g. “journal article” or “database”). When the GI value was derived through an arithmetic mean of several contributing values, or when a logical zero was applied (Acquisition type descriptor = “created within host system”), no literature references for the original values could be stored.

According to the EuroFIR controlled vocabularies, all stored GI values received the descriptor “ratio” (Unit thesaurus) since GI is an index number. The descriptor “not applicable” (Matrix unit thesaurus indicating the mode of expression) was applied for all stored GI values. The thesauri of Component and Method Indicator lacked descriptors applicable for GI values.

We also compared the value origin and derivation methods across all studied carbohydrate factors in the FFQ method (see Appendix 2). This analysis was performed separately for composite foods (mainly dishes) and basic ingredients. The GI differed from the other carbohydrate factors because analysed values were available for composite foods. This reflects the fundamental difference between GI and the other carbohydrate factors. GI is a food-level property of carbohydrate-containing foods.

5.2 FFQ VALIDITY (II)

5.2.1 INTAKE LEVELS AND CROSS-CLASSIFICATION OF SUBJECTS

The subjects of the FFQ validation study were, on average, 55 and 52 years old (age range 25-74 years), and their mean BMI was 27.2 and 26.7 kg/m² in men and women, respectively. Altogether, 37% of both women and men represented the group with the highest educational level. Validation results for carbohydrate factors are shown in Tables 12-14. Results for protein and fat are shown for sake of comparison in each table.

Relative to FRs, the FFQ consistently overestimated energy-adjusted intakes of the studied carbohydrate fractions (total carbohydrate, starch, total sugars, fructose, lactose, sucrose, dietary fibre, insoluble dietary fibre, soluble polysaccharides) and dietary GL in both sexes (Table 12). A similar pattern of overestimation was evident for crude absolute intakes (data not shown). Overestimation seemed to be lowest for total carbohydrate, starch, and GL, and highest for fructose and lactose. Generally, the same food groups explained some 90% of the total carbohydrate, fructose, sucrose, and dietary fibre intakes in FFQs and FRs (see Appendix 3).

Energy-adjusted correlations in men ranged from 0.27 (total sugars) to 0.70 (lactose) and in women from 0.37 (total sugars) and 0.69 (lactose) (Table 13). Overall, in 9 out of 11 carbohydrate factors the correlation of 0.40 was exceeded. Crude correlations for food groups contributing to intake of carbohydrate fractions ranged in men from 0.36 (fruit juice) to 0.69 (milk products) and in women from 0.30 (sugar-sweetened juice) to 0.75 (alcoholic beverages) (see Appendix 4). The extent of convergent classification of subjects into carbohydrate factor quintiles by the two methods (same or adjacent quintile) was on average 73% in both men (range from 62% for total sugars to 83% for lactose) and women (range from 64% for total sugars to 83% for lactose). The highest level of gross misclassification in men emerged for total sugars (5.5%) and in women for fructose (3.8%).

Table 12. *Mean daily energy-adjusted nutrient intakes, dietary glycaemic index and load based on food frequency questionnaires (FFQs) and two 3-day food records (FRs) in women and men.*

Dietary factor (g/day) ²	FFQ	FR	FFQ% of FR ¹	
	Mean (SD)	Mean (SD)	% Mean	95% CI
Women (n=292)				
Energy (MJ/day) ³	9.3 (3.0)	7.4 (1.7)	131	125-137
Total carbohydrate	279 (35)	223 (30)	126	124-128
Starch	145 (29)	118 (22)	125	122-128
Total sugars	132 (30)	104 (23)	132	128-136
Fructose	23 (10)	15 (6.5)	175	162-187
Lactose	25 (13)	16 (11)	225	168-283
Sucrose	59 (19)	51 (18)	126	121-132
Dietary fibre	32 (9.0)	23 (6.5)	143	138-147
Insoluble dietary fibre	22 (6.3)	16 (4.6)	141	137-146
Soluble polysaccharide	7.5 (2.3)	5.4 (1.7)	145	140-150
Dietary glycaemic index	62 (3.8)	63 (3.9)	99	98-99
Dietary glycaemic load	173 (24)	141 (20)	124	122-127
Protein	101 (14)	77 (11)	132	130-134
Fat	82 (13)	69 (11)	121	119-124
Men (n=218)				
Energy (MJ/day) ³	11.7 (4.0)	9.3 (2.3)	130	124-137
Total carbohydrate	268 (33)	215 (28)	126	124-128
Starch	148 (28)	122 (27)	125	121-129
Total sugars	119 (29)	91 (23)	137	131-143
Fructose	19 (9.6)	12 (6.6)	185	167-204
Lactose	25 (14)	17 (10)	183	165-201
Sucrose	50 (18)	41 (18)	139	129-150
Dietary fibre	27 (7.5)	22 (7.6)	133	128-138
Insoluble dietary fibre	20 (5.2)	16 (5.5)	133	128-139
Soluble polysaccharide	6.2 (1.8)	4.9 (1.7)	135	130-141
Dietary glycaemic index	65 (4.0)	66 (4.7)	99	98-100
Dietary glycaemic load	174 (23)	142 (19)	124	121-126
Protein	103 (14)	81 (13)	130	127-133
Fat	82 (12)	68 (11)	122	119-125

SD, standard deviation

¹ Mean ratio of the two dietary methods on the population level and is calculated as FFQ/FR x 100 with 95% confidence intervals (CI).

² Energy-adjusted daily values (g/day).The residual method was used for energy adjustment. Glycaemic index and glycaemic load are unitless.

³ Crude values (no adjustments).

Table 13. Between-method Spearman rank-correlation coefficients (r_s) and quintile cross-classification of daily nutrient intakes and dietary glycaemic index and load¹

	Women			Men		
	r_s	same ± 1 quintile (%)	opposite quintile (%) ²	r_s	same ± 1 quintile (%)	opposite quintile (%) ²
<i>Dietary factor (g/day)</i> ³						
Total carbohydrate	0.54	75	2.1	0.51	70	1.8
Starch	0.48	72	1.7	0.41	67	2.3
Total sugars	0.37	64	3.1	0.27	62	5.5
Fructose	0.39	70	3.8	0.44	73	3.2
Lactose	0.69	83	1.0	0.70	83	0.5
Sucrose	0.46	70	2.4	0.49	77	3.7
Dietary fibre	0.58	76	1.0	0.67	80	0.9
Insoluble dietary fibre	0.62	78	1.0	0.66	78	1.4
Soluble Polysaccharides	0.55	76	1.4	0.66	82	1.4
Dietary glycaemic index	0.41	69	3.1	0.31	65	4.1
Dietary glycaemic load	0.49	72	1.4	0.43	69	1.0
Protein	0.42	70	3.8	0.36	65	0.9
Fat	0.38	63	2.4	0.45	66	0.9

¹ Compared methods: food frequency questionnaire and two 3-day food records.

² Disagreement by four quintiles (gross misclassification).

³ Energy-adjusted intakes (g/day). The residual method was used for energy-adjustment. Glycaemic index and glycaemic load are unitless.

5.2.2 FACTORS AFFECTING BETWEEN-METHOD AGREEMENT

In women, a relationship between intake level (indicated by method mean FFQ+FR/2 in g/day) and between-method agreement (indicated by difference FFQ-FR in g/day) was observed for all carbohydrate factors other than sucrose and dietary GI (Table 14). For example, a 1 g/day increase in dietary fibre intake was associated with a 0.39 g/day increment in the difference between FFQ and FRs in women. This indicates a relationship between level of intake and measurement error in FFQs relative to FRs. In men, this phenomenon was observed for total carbohydrate ($\beta=0.21$; $P=0.006$), total sugars ($\beta=0.36$; $P=0.0005$), fructose ($\beta=0.54$; $P<0.0001$), lactose ($\beta=0.39$; $P<0.0001$), and dietary GI ($\beta=-0.24$; $P=0.007$) and GL ($\beta=0.20$; $P=0.016$). This suggests that disagreement between the methods was dependent on the intake level for most of the studied carbohydrate factors, especially in women.

Age was associated with the between-method agreement in women for all studied carbohydrate factors, except starch, lactose, and insoluble dietary fibre (Table 14). In most cases, an increase in age was associated with a significant increment in the difference between FFQ and FR, indicating bias towards higher intake values with FFQs relative to FRs. Dietary GI was the only carbohydrate factor for which the

increase in age was associated with a decrement in the between-method difference ($\beta=-0.04$). In men, corresponding associations between age and the between-method difference were observed for lactose ($\beta=-0.13$; $P=0.011$) and dietary GL ($\beta=0.33$; $P=0.005$).

Regarding education, belonging to a lower educational group (relative to the highest) was associated with decrements in the difference between FFQ and FR in both sexes. This indicates bias towards underestimation of intake by the FFQ in lower educated subjects relative to higher educated subjects. In women, this was observed for total carbohydrate, starch, lactose, and dietary GL (lowest educational group relative to the highest). In men, belonging to the middle educational group (relative to the highest) was associated with the between-method difference only for dietary fibre ($\beta=-2.22$; $P=0.0241$) and insoluble dietary fibre ($\beta=-1.65$; $P=0.0227$).

Associations between BMI and between-method agreement were absent in both sexes.

Table 14. *Associations of daily intake and subject characteristics with between-method difference for energy-adjusted nutrient intakes and dietary glycaemic index and load in 292 women.¹*

Dietary factor (g/day)	Dietary factor difference FFQ-FR ²					
	Mean (FFQ+FR/2)		Age ³		Low education ⁴	
	β^5	P-value	β	P-value ⁶	β	P-value ⁶
Total carbohydrate	0.20	0.0022 **	0.59	<.0001 ***	-10.55	0.0184 *
Starch	0.38	<.0001 ***	0.05	0.6969	-12.08	0.0013 **
Total sugars	0.36	<.0001 ***	0.49	0.0001 **	1.55	0.7068
Fructose	0.60	<.0001 ***	0.09	0.0181 *	2.17	0.0842
Lactose	0.29	<.0001 ***	-0.02	0.6516	-3.21	0.0233 *
Sucrose	0.09	0.2341	0.24	0.0054 **	0.18	0.9487
Dietary fibre	0.39	<.0001 ***	0.06	0.0425 *	-0.20	0.8440
Insoluble dietary fibre	0.39	<.0001 ***	0.04	0.1017	-0.47	0.4810
Soluble polysaccharides	0.36	<.0001 ***	0.02	0.0478 *	0.12	0.6512
Dietary glycaemic index	-0.03	0.7298	-0.04	0.0196 *	-0.78	0.1862
Dietary glycaemic load	0.28	<.0001 ***	0.25	0.0121 *	-9.00	0.0049 **
Protein	0.35	<.0001 ***	-0.14	0.0148 *	0.59	0.7545
Fat	0.25	0.0011 **	-0.21	0.0003 **	4.18	0.0244 *

¹ For results in men (n=218), see text.

² Based on daily energy-adjusted values (g/day). The residual method was used for energy adjustment; FFQ, food frequency questionnaire; FR, two 3-day food records.

³ Continuous variable (years).

⁴ Categorical variable. Reference group: high education. Due to missing values n=289.

⁵ Regression coefficient (all such).

⁶ In cases where the mean intake (FFQ+FR/2) was significantly associated with the difference (FFQ-FR), the mean was included in the model.

Statistical significance levels: * $P<0.05$; ** $P<0.01$; *** $P<0.0001$ (H_0 : slope=0); all such values.

5.3 SUGAR INTAKE AND OTHER DIETARY COMPONENTS (III)

Table 15 shows background and nutritional characteristics of Study III subjects (n=4842). Compared with women, men were older, less often low educated, and more often current smokers. An equal proportion of men and women (about 19%) were physically inactive. Intakes of total carbohydrate, naturally occurring and added sugars (both based on sucrose and fructose) and dietary fibre were on average lower, and fat intake higher in men compared with women. Average protein intake was equal among the sexes. The median added sugar intakes across quartiles ranged from 4.7 E% to 12.1 E% in women, and from 4.1 E% to 11.8 E% in men. Corresponding ranges for naturally occurring sugar were from 2.9 E% to 10.2 E% in women, and from 1.9 E% to 8.0 E% in men.

Table 15. *Characteristics and nutrient intakes of subjects in Study III.*

	Women (n=2599)		Men (n=2243)	
	Mean / %	95 % CI	Mean / %	95% CI
Background and anthropometrics				
Age (years)	52.0	51.4, 52.5	53.2	52.6, 53.7
Low educated subjects (%)	31.5	29.7, 33.3	27.3	25.4, 29.1
Current smokers (%)	14.6	13.2, 16.0	20.5	18.9, 22.2
Physically inactive subjects (%)	18.9	17.4, 20.4	18.5	16.9, 20.1
Body mass index (kg/m ²)	26.8	26.6, 27.0	27.2	27.0, 27.3
Waist circumference (cm)	86.8	86.3, 87.3	96.5	96.0, 97.0
Energy under-reporters (%)	19.4	17.9, 21.0	22.6	20.8, 24.3
Nutrient intake (g/day)¹				
Total carbohydrate	284	282, 285	271	270, 273
Total sucrose and fructose	85.1	84.1, 86.1	72.6	71.5, 73.7
Naturally occurring sugar ²	36.4	35.6, 37.1	27.8	27.1, 28.6
Naturally occurring sucrose	16.3	16.0, 16.7	12.5	12.2, 12.9
Added sugar ²	48.8	48.0, 49.6	44.5	43.7, 45.4
Added sucrose	44.5	43.7, 45.2	40.4	39.7, 41.2
Dietary fibre	32.1	31.7, 32.4	26.7	26.4, 27.1
Protein	103	102, 103	103	103, 104
Fat	81.9	81.4, 82.4	83.9	83.4, 84.5
Nutrient intake (E %)				
Carbohydrate	50.2	50.0, 50.5	47.7	47.4, 47.9
Total sucrose and fructose	14.6	14.4, 14.8	12.6	12.4, 12.8
Naturally occurring sugar ²	6.3	6.2, 6.4	4.7	4.6, 4.9
Added sugar ²	8.3	8.1, 8.4	7.8	7.7, 8.0
Dietary fibre ³	13.8	13.7, 14.0	11.1	11.0, 11.3
Protein	17.8	17.7, 17.9	17.7	17.6, 17.8
Fat	30.6	30.4, 30.7	31.7	31.5, 31.9

CI, confidence interval

¹ Daily intake values are energy-adjusted using the residual method.

² Estimate based on sucrose and fructose.

³ Expressed as g/1000 kcal.

5.3.1 SUGAR INTAKE AND SUBJECT CHARACTERISTICS

In women, added sugar intake (i.e. estimate based on sucrose and fructose) was inversely associated with age, WC, and the proportion of energy under-reporters (Table 16). Similar results were found in men, including inverse associations between added sugar and BMI and the proportion of current smokers. Overall, directions of associations were similar for naturally occurring sugar (i.e. estimate based on sucrose and fructose), except that naturally occurring sugar intake was positively associated with age (P for trend <0.01), and high naturally occurring sugar consumers were higher educated than low consumers ($P<0.01$) in both sexes (data not shown). BMI and WC were not associated with naturally occurring sugar in men (P for trends 0.59 and 0.33, respectively), whereas inverse associations were evident in women (P for trends 0.04 and 0.01, respectively; data not shown).

With increasing added sugar intakes, total carbohydrate and total sugar intakes increased, whereas intakes of naturally occurring sugar, dietary fibre, protein, and fat decreased (Table 16). For nutrients, results remained unchanged when further adjusting for leisure-time physical activity, education, smoking, and BMI (data not shown). The exclusion of energy under-reporters did not change the results (data not shown). Compared with added sugar, the directions of associations were similar between naturally occurring sugar and nutrients. However, energy (P for trends <0.05) and dietary fibre (P for trends <0.001) intakes increased, and the intake of added sugar decreased (P for trends <0.02) with increasing naturally occurring sugar intakes in both sexes (data not shown).

5.3.2 SUGAR INTAKE AND FOOD GROUPS

The associations between added sugar and other food groups in the diet were overall similar in women and men (Table 17). However, the magnitudes of shifts in food group intakes between the lowest quartile and the highest quartile seemed to differ between the sexes.

Overall, added sugar intake was positively associated with its food sources (sugar and syrups, sweets and chocolate, and SSB) (Table 17). For example, the intake of SSB was 10-fold higher in the highest quartile of added sugar than in the lowest quartile. Fruit and vegetable intakes were 1.1-1.4-fold lower in the highest added sugar intake quartile than in the lowest quartile. Rye, potato, meat, fish, vegetable margarine, and alcoholic beverage intakes decreased with increasing added sugar intakes, whereas wheat, butter, and milk product intakes (women only) increased. Further adjustment for leisure-time physical activity, education, smoking, and BMI did not change the results in either sex. The only exception was that the positive association between added sugar intake and coffee/tea consumption became statistically significant in men (P for trend=0.02).

In general, the directions of associations between naturally occurring sugar and food groups were contrary to the results for added sugar in terms of added sugar sources and naturally occurring sugar sources. Rye, wheat, potato, meat, butter, and vegetable margarine (women only) intakes decreased with increasing naturally occurring sugar intakes (all P -values for trends <0.03).

Table 16. Associations between added sugar intake and subject characteristics and nutrient intakes in Study III.¹

	Added sugar intake quartiles ²				
	Q1 ³	Q4 ⁴	Q1-Q4		
	Mean / %	Mean / %	Difference	Direction ⁵	P trend ⁶
Women (n=2599)					
Age (years)	55.1	50.0	5.1	↓	<0.0001
Low educated subjects (%)	31.6	35.0	3.4	-	NS
Current smokers (%)	17.5	13.4	4.1	-	NS
Physically inactive subjects (%)	18.5	21.5	3.0	-	NS
Body mass index (kg/m ²)	27.2	26.5	0.7	-	NS
Waist circumference (cm)	88.4	85.8	2.6	↓	0.003
Energy under-reporters (%) ⁷	22.8	19.2	3.6	↓	0.022
Energy (MJ/day)	9.30	9.56	0.26	-	NS
Total carbohydrate (g/day)	270	300	-30.0	↑	<0.0001
Total sucrose+fructose (g/day)	67.3	109	-41.7	↑	<0.0001
Naturally occurring sugar (g/day) ⁸	40.4	32.7	7.7	↓	<0.0001
Dietary fibre (g/day)	35.5	28.8	6.7	↓	<0.0001
Protein (g/day)	111	93.4	17.6	↓	<0.0001
Fat (g/day)	83.7	79.6	4.1	↓	<0.0001
Men (n=2243)					
Age (years)	54.5	52.2	2.0	↓	0.003
Low educated subjects (%)	25.0	30.6	5.6	-	NS
Current smokers (%)	24.3	18.1	6.2	↓	0.041
Phys. inactive subjects (%)	21.8	17.1	4.7	-	NS
Body mass index (kg/m ²)	27.8	26.4	1.4	↓	<0.0001
Waist circumference (cm)	98.5	94.2	4.3	↓	<0.0001
Energy under-reporters (%) ⁷	27.5	21.2	6.3	↓	0.013
Energy (MJ/day)	11.36	11.67	0.31	-	NS
Total carbohydrate (g/day)	255	290	-35.0	↑	<0.0001
Total sucrose+fructose (g/day)	51.2	98.0	-46.8	↑	<0.0001
Naturally occurring sugar (g/day) ⁸	28.6	25.8	2.8	↓	0.009
Dietary fibre (g/day)	28.1	24.9	3.2	↓	<0.0001
Protein (g/day)	110	94.5	15.5	↓	<0.0001
Fat (g/day)	85.4	80.8	4.6	↓	<0.0001

¹ Nutrient intakes are energy- and age-adjusted, except energy, which is only age-adjusted.

² Added sugar calculated as [total sucrose + fructose] – [natur. occurring sucrose + fructose].

³ Q1, Lowest quartile: median added sugar intake 27.6 g/day (women) and 23.7 g/day (men).

⁴ Q4, Highest quartile: median added sugar intake 71.9 g/day (women) and 66.4 g/day (men).

⁵ Direction of association: ↓=negative, ↑=positive, - =no association.

⁶ Generalized linear modelling (continuous variables), Chi-square test (binary variables). Trend analyses of nutritional characteristics adjusted for age and energy intake (except in case of energy as dependent variable, the model was only age-adjusted). NS=non-significant.

⁷ Energy under-reporting based on Goldberg cut-off value (≤ 1.14) for ratio of reported energy intake to predicted basic metabolic rate (Goldberg et al. 1991).

⁸ Naturally occurring sugar calculated as [sucrose+ fructose] from the ingredient groups fruits, berries, 100% fruit juice, and vegetables.

Table 17. Associations between added sugar and food group intakes (geometric means).

	Added sugar intake quartiles ¹				
	Q1 ² Mean	Q4 ³ Mean	Q1-Q4 Difference	Direction ⁴	P trend ^{4, 5}
Food intake (g/day)					
Women (n=2599)					
Sugars and syrups	7.4	18.3	-10.9	↑	<.0001
Sweets and chocolate	6.0	16.6	-10.6	↑	<.0001
SSB ⁶	6.8	71.8	-65	↑	<.0001
Fruits	193	141	52	↓	<.0001
Berries	27.5	34.0	-6.6	↑	<.0001
Fruit juices (100%)	26.1	26.7	-0.6	-	0.88
Vegetables	339	234	105	↓	<.0001
Rye	59.2	41.3	17.9	↓	<.0001
Wheat	52.1	59.0	-6.9	↑	<.0001
Potatoes, potato products	108	92.7	15.3	↓	<.0001
Meat, meat products	144	111	33	↓	<.0001
Fish, fish products	39.8	28.4	11.4	↓	<.0001
Milk, milk products	450	503	-53	↑	0.001
Butter	4.1	5.4	-1.3	↑	<.0001
Vegetable margarine	8.3	6.8	1.5	↓	0.0003
Coffee and tea	446	405	41	-	0.08
Alcoholic beverages	31.0	15.0	16	↓	<.0001
Men (n=2243)					
Sugars and syrups	8.4	25.4	-17	↑	<.0001
Sweets and chocolate	5.4	14.1	-8.7	↑	<.0001
SSB ⁶	12.9	134	-121.1	↑	<.0001
Fruits	117	104	13	↓	0.033
Berries	16.0	25.4	-9.4	↑	<.0001
Fruit juices (100%)	44.6	54.7	-10.1	-	0.07
Vegetables	248	188	60	↓	<.0001
Rye	58.6	46.4	12.2	↓	<.0001
Wheat	67.4	78.0	-10.6	↑	<.0001
Potatoes, potato products	167	142	25	↓	<.0001
Meat, meat products	219	170	49	↓	<.0001
Fish, fish products	53.9	40.2	13.7	↓	<.0001
Milk, milk products	545	532	13	-	0.47
Butter	5.4	6.9	-1.5	↑	<.0001
Vegetable margarine	10.3	8.1	2.2	↓	0.0009
Coffee and tea	425	464	-39	-	0.12
Alcoholic beverages	101	53.3	47.7	↓	<.0001

¹ Added sugar calculated as [total sucrose + fructose] – [naturally occurring sucrose + fructose].

² Q1, Lowest quartile: median added sugar intake 27.6 g/day (women) and 23.7 g/day (men).

³ Q4, Highest quartile: median added sugar intake 71.9 g/day (women) and 66.4 g/day (men).

⁴ Direction of association: ↓=negative, ↑=positive, - =no association. Age- and energy-adjusted.

⁵ P-values for trend from generalized linear modelling (sugar intake quartile medians as continuous independent variables and each food group as dependent variable at a time).

⁶ Sugar-sweetened beverages from FFQ items “berry juice” and sugar-sweetened soft drinks.

5.4 CARBOHYDRATE FACTORS AND OBESITY (IV)

Of the subjects included in Study IV (n=12 342), 21-25% were classified as obese (BMI ≥ 30 kg/m²) (Table 18). Relative to them, the non-obese were on average younger (DILGOM and Health 2000), more often men (DILGOM and Health 2000), exercised more during leisure-time (DILGOM and HBCS), were more frequently current smokers (Health 2000), and were more educated. Energy under-reporting was more common in the obese than in the non-obese. Average daily energy intake did not differ between the BMI groups, and nutrient intakes and dietary GI and GL differed slightly.

5.4.1 OVERALL ASSOCIATIONS

The three models on the association between carbohydrate factors and obesity yielded fairly similar results (Table 19). Model 3 was regarded as the main model of this cross-sectional analysis presenting the situation where the effect of total energy intake is fully eliminated. In Model 3, the likelihood of being obese was 47% lower in the highest total sucrose intake quartile than the lowest quartile (P for trend <0.0001). Total carbohydrate and dietary GL were inversely associated with the risk of obesity (P for trends <0.0001). The likelihood of being obese was 22% higher in the highest lactose intake quartile than in the lowest quartile (P for trend 0.001). No associations between fibre or dietary GI and obesity risk were found (P-values for trends 0.20 and 0.15, respectively). There was no statistically significant heterogeneity between studies. Study-specific ORs with 95% CIs for highest versus lowest carbohydrate factor quartiles are shown in Figure 6.

When repeating the analyses with elevated WC as the outcome measure, similar results as for the BMI outcome were obtained (data not shown). However, an inverse association between fibre and elevated WC (OR 0.80; 95% CI 0.71-0.90 for highest vs. lowest quartile; $P<0.001$) was found. The exclusion of energy under-reporters (n=3264, 26%) did not change the results observed for overall obesity based on the cut-off BMI ≥ 30 kg/m².

5.4.2 EFFECT MODIFICATION BY SEX AND FRUIT INTAKE

Regarding effect modification by sex, an inverse association between GI and obesity was evident in men (Model 3; OR 0.76; 95% CI 0.62-0.93 for highest vs. lowest quartile, $P=0.12$), but not in women (Model 3; OR 1.02; 95% CI 0.85-1.22 for highest vs.. lowest quartile, $P=0.63$) (P for interaction=0.03). The inverse association between GL and obesity appeared stronger in men (Model 3; OR 0.55; 95% CI 0.45-0.67 for highest vs. lowest quartile; $P<0.0001$) than in women (Model 3; OR 0.72; 95% CI 0.61-0.85 for highest vs. lowest quartile; $P<0.0001$) (P for interaction=0.04).

Fruit intake appeared to be an effect modifier of the sucrose-obesity association (P for interaction=0.02). The inverse association between sucrose and obesity was stronger in the high fruit intake group (n=6172; OR 0.45; 95% CI 0.37-0.55 for highest vs. lowest quartile; $P<0.0001$) than in the low fruit intake group (n=6170; OR 0.62; 95% CI 0.52-0.74 for highest vs. lowest quartile; $P<0.0001$). Across studies, the medians of fruit and berry intake were in the range of 280-354 g/day in the high intake group, and 73-112 g/day in the low intake group.

Table 18. Sociodemographic, lifestyle, and nutritional characteristics of study subjects by body mass index group in Study IV.¹

	DILGOM			HBCS			Health 2000		
	BMI < 30 n=3810	BMI ≥ 30 n=1032	P ²	BMI < 30 n=1483	BMI ≥ 30 n=496	P ²	BMI < 30 n=4289	BMI ≥ 30 n=1232	P ²
Age (years)	52 (13.6)	56 (12.3)	0.002	62 (2.9)	62 (3.0)	0.01	50 (12.8)	54 (12.1)	0.037
Females (%)	53	58	<0.0001	52	59	0.98	53	57	<0.0001
Physically active (%)	29	21	<0.0001	28	18	<0.0001	27	27	0.76
Current smokers (%)	18	16	0.104	24	22	0.25	29	22	<0.0001
Education (years)	12.9 (4.0)	11.6 (3.7)	<0.0001	12.4 (3.7)	11.6 (3.5)	0.0001	11.9 (4.0)	10.4 (3.7)	<0.0001
WC (cm)	86.7 (10.2)	108.3 (11.4)	<0.0001	90.7 (9.9)	110 (10.6)	<0.0001	87.9 (10.3)	108.3 (10.3)	<0.0001
Energy under-reporters (%)	18	31	<0.0001	26	42	<0.0001	27	42	<0.0001
Energy (MJ/day)	10.5 (3.7)	10.6 (4.1)	0.30	9.4 (3.4)	9.3 (3.6)	0.74	9.6 (3.3)	9.5 (3.5)	0.78
Total carbohydrate (g/day)	279 (35)	275 (35)	0.003	244 (35)	238 (36)	0.001	234 (30)	232 (32)	0.004
Sucrose (g/day) ³	58.1 (20.7)	54.1 (20.8)	<0.0001	49.7 (19.0)	46.3 (17.9)	<0.001	47.0 (16.8)	43.1 (17.0)	<0.0001
Lactose (g/day)	24.8 (14.3)	26.3 (15.3)	0.003	21.3 (12.9)	23.2 (14.5)	0.01	23.0 (13.3)	25.0 (14.0)	<0.0001
Dietary fibre (g/day)	29.5 (9.0)	29.8 (9.1)	0.34	25.9 (8.4)	25.6 (8.5)	0.40	23.8 (7.2)	24.3 (7.2)	0.36
Dietary glycaemic index	63.1 (4.3)	63.4 (4.2)	0.08	63.9 (5.1)	63.3 (4.6)	0.03	64.9 (4.2)	64.9 (4.1)	0.98
Dietary glycaemic load	173 (24)	172 (23)	0.21	153 (21)	149 (23)	<0.0001	155 (22)	153 (23)	0.02
Protein (g/day)	102 (14)	105 (15)	<0.0001	87.5 (12.9)	91.6 (13.5)	<0.0001	90.3 (11.8)	93.5 (12.6)	<0.0001
Fat (g/day)	82.7 (13.1)	83.5 (13.1)	0.08	77.0 (12.6)	79.4 (12.8)	<0.0001	88.2 (11.9)	88.7 (12.6)	0.18
Alcohol (ethanol, g/day)	7.4 (10.5)	7.0 (11.3)	0.25	9.7 (13.1)	7.8 (11.7)	0.004	5.5 (9.0)	4.8 (8.6)	0.01
Fruit intake (g/day) ⁴	275 (234)	259 (234)	0.047	282 (265)	262 (239)	0.14	213 (205)	216 (211)	0.63

BMI, body mass index WC, waist circumference

1 Daily nutrient intakes (g/day), dietary GI and GL (unit less) are energy-adjusted using the residual method. Values are means (SD) or %. BMI grouping: BMI<30 kg/m²= non-obese and BMI ≥ 30 kg/m²=obese;

2 P-value for difference between groups (independent samples t-test for continuous variables and Chi-square test for binary background variables).

3 Total sucrose including both naturally occurring and added sucrose.

4 Unadjusted crude intake (includes berries).

Table 19. Pooled odds ratios and 95% confidence intervals for obesity by quartiles of carbohydrate factors¹.

	Model 1 ^{2,3}	Model 2 ^{2,4}	Model 3 ^{2,5}
Total carbohydrate (g/day)			
Quartile 2	0.82 (0.73, 0.92)	0.81 (0.72, 0.92)	0.81 (0.72, 0.92)
Quartile 3	0.70 (0.62, 0.79)	0.70 (0.62, 0.79)	0.70 (0.62, 0.79)
Quartile 4	0.65 (0.57, 0.73)	0.65 (0.57, 0.74)	0.65 (0.57, 0.74)
P (trend) ⁶	<0.001	<0.001	<0.001
P (heterogeneity) ⁷	0.74	0.92	0.92
Sucrose (g/day)⁸			
Quartile 2	0.76 (0.68, 0.86)	0.76 (0.67, 0.85)	0.75 (0.67, 0.85)
Quartile 3	0.61 (0.53, 0.72)	0.62 (0.52, 0.73)	0.61 (0.52, 0.72)
Quartile 4	0.55 (0.48, 0.62)	0.54 (0.47, 0.61)	0.53 (0.47, 0.61)
P (trend)	<0.001	<0.001	<0.001
P (heterogeneity)	0.25	0.13	0.16
Lactose (g/day)			
Quartile 2	1.06 (0.92, 1.21)	1.08 (0.95, 1.22)	1.07 (0.94, 1.22)
Quartile 3	1.16 (1.02, 1.31)	1.12 (0.98, 1.27)	1.11 (0.97, 1.26)
Quartile 4	1.24 (1.10, 1.40)	1.22 (1.08, 1.39)	1.22 (1.08, 1.39)
P (trend)	<0.001	0.001	0.001
P (heterogeneity)	0.93	0.91	0.89
Dietary fibre (g/day)			
Quartile 2	0.86 (0.76, 0.97)	0.91 (0.80, 1.03)	0.90 (0.79, 1.03)
Quartile 3	0.82 (0.69, 0.97)	0.86 (0.76, 0.98)	0.86 (0.75, 0.98)
Quartile 4	0.82 (0.71, 0.95)	0.92 (0.81, 1.05)	0.92 (0.80, 1.05)
P (trend)	0.005	0.21	0.20
P (heterogeneity)	0.34	0.62	0.61
Dietary glycaemic index			
Quartile 2	0.98 (0.87, 1.11)	0.96 (0.85, 1.09)	0.96 (0.85, 1.09)
Quartile 3	0.94 (0.81, 1.08)	0.90 (0.78, 1.03)	0.90 (0.78, 1.04)
Quartile 4	0.99 (0.87, 1.12)	0.91 (0.80, 1.04)	0.92 (0.81, 1.05)
P (trend)	0.71	0.10	0.15
P (heterogeneity)	0.44	0.56	0.48
Dietary glycaemic load			
Quartile 2	0.83 (0.73, 0.93)	0.81 (0.68, 0.96)	0.81 (0.69, 0.95)
Quartile 3	0.75 (0.67, 0.85)	0.75 (0.66, 0.85)	0.75 (0.66, 0.85)
Quartile 4	0.66 (0.58, 0.75)	0.64 (0.56, 0.73)	0.64 (0.56, 0.73)
P (trend)	<0.001	<0.001	<0.001
P (heterogeneity)	0.29	0.34	0.32

¹ Obesity is defined as BMI ≥ 30 kg/m². Carbohydrate factors energy-adjusted (residual method).

² The lowest carbohydrate factor quartile was used as the reference in all analyses (OR 1.00).

³ Adjusted for age and sex.

⁴ Adjusted for age, sex, education, leisure-time physical activity, and smoking.

⁵ Adjusted for age, sex, education, leisure-time physical activity, smoking, and energy intake.

⁶ P-value for linear trend across quartiles (Wald test); all such values.

⁷ P-value for heterogeneity between included studies (Q statistic); all such values.

⁸ Total sucrose including both naturally occurring and added sucrose.

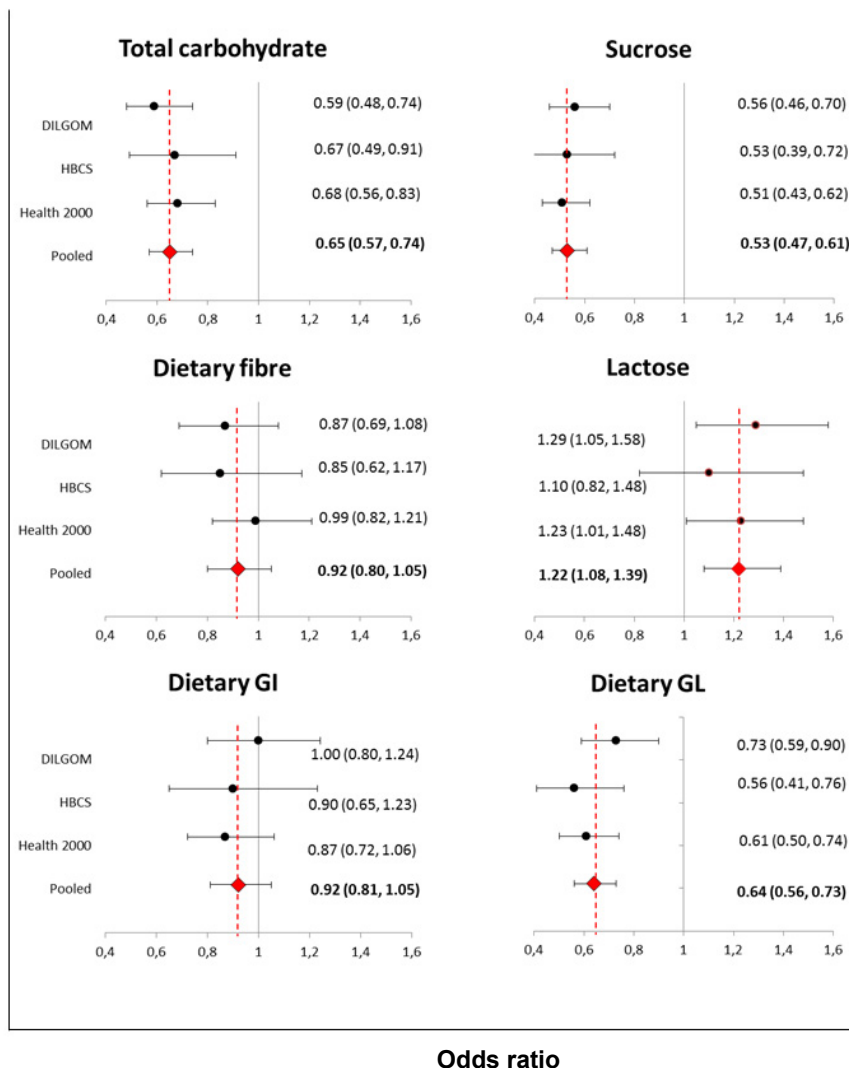


Figure 6 Study-specific and pooled multivariate odds ratios (ORs) and 95% confidence intervals (95% CIs) of obesity (BMI ≥ 30 kg/m²) for the highest carbohydrate factor quartile relative to the lowest quartile. The black dots indicate the study-specific ORs; the red square and the dashed line represent the pooled ORs, and the horizontal lines represent the 95% CIs. Sucrose refers to total sucrose and includes both naturally occurring and added sucrose. GI= glycaemic index; GL=glycaemic load; DILGOM=Dietary, Lifestyle, and Genetic determinants of Obesity and the Metabolic syndrome Study; HBCS=Helsinki Birth Cohort Study; Health 2000=Health 2000 Health Examination Survey.

6 DISCUSSION

Dietary carbohydrates have various roles in maintaining long-term human health. Glycaemic carbohydrates, including sugars, provide energy. Dietary fibre contributes to gut health maintenance and helps in achieving optimal satiety. The blood glucose-raising potential of carbohydrate-containing foods and their overall blood glucose responses have been quantified in the dietary GI and GL measures. Thus far, the results on the associations between these carbohydrate factors and obesity have been inconclusive. Our meta-analysis of three Finnish cross-sectional studies found that most dietary carbohydrates were inversely associated with obesity (IV). In the changing food environment, the role of added sugars from all dietary sources in adult diets requires clarification. In this thesis, several significant associations between added sugars and other dietary components emerged (III).

The constantly changing food environment represents a methodological challenge to nutritional research. An up-to-date methodological basis enables investigation on dietary carbohydrate factors and their role in overall nutrition and long-term health of the general population. This basis includes verifying food composition database quality and the validity of dietary intake assessment methods, with FFQs being the prevailing method in nutritional epidemiology. This thesis showed that controlled vocabularies established within the EuroFIR Network are suitable for documenting food GI values in a standardized FCDB framework (I). The FFQ validation study provided evidence that the FFQ designed for use in the Finnish adult population is reasonably valid in measuring most dietary carbohydrates (II).

6.1 MAIN STRENGTHS AND LIMITATIONS

Study population and measurements

The overall strength of the four studies included in this thesis was their reliance on population-based data gathered in Finnish adults (I-IV). The FINRISK 2007 Study (including FINDIET 2007) and the DILGOM Study were conducted in five large geographical areas with both urban and rural locations based on stratified random sampling from the population register. The Health 2000 Survey (IV) sampling strategy covered the whole of mainland Finland.

Participation rates in health surveys have overall declined during the past decades in all European countries, including Finland (Mindell et al. 2015). In the studies included here, participation rates in health examinations were between 63% (FINDIET 2007) and 84% (Health 2000), which is good in international comparison. This suggests good generalizability of our findings to the Finnish adult population. On the other hand, recent analysis of the association between socioeconomic status and non-participation in the FINRISK studies during 1987 and 2012 revealed a marked decline in participation in low-educated adults (Reinikainen et al. 2017). Individuals with higher education are shown to have overall healthier diets (Hulshof

et al. 2003, Ovaskainen et al. 2010). This should be taken into account in interpretation of our findings and evaluation of their generalizability.

All population-based studies used in this thesis included a health examination with thorough health questionnaires that collected information on education and lifestyle factors such as smoking and physical activity. This made the consideration of central confounding factors possible in our analyses (III, IV). Despite this, residual confounding may remain. This is also due to the fact that some confounders, such as leisure-time physical activity, are likely to be inaccurately measured with questionnaires. The carbohydrate-obesity relationship (IV) may especially be affected by this, as energy expenditure is a determinant of energy balance. However, the physical activity questions used in the questionnaires of the DILGOM Study, HBCS, and Health 2000 Survey have shown good criterion validity against morbidity and mortality (Hu et al. 2007) and a moderate correlation with accelerometer device counts in working-aged adults (Fagt et al. 2011).

Strengths and limitations of individual studies

Strengths of this thesis include the comprehensiveness of the food list, for which GI values were applied (I). Both 48-hour DR and two 3-day FRs were used to identify the foods consumed by Finnish adults. Moreover, the GI values for the consumed foods were largely based on the previous GI database compiled for use in Finnish men of the ATBC Study (Similä et al. 2009). In that study efforts were directed to formulating the minimum methodological criteria for selecting GI values. This, together with the application of controlled value documentation vocabularies of EuroFIR provides good grounds for GI-related research. As a limitation, not all technical features of the EuroFIR value documentation were adopted in the Finnish national FCDB Fineli at the time that our study was conducted. Therefore, only a limited number of the fundamental dimensions of the value documentation were covered.

The FFQ validated in this thesis (II) from the perspective of carbohydrate factors represents one loop in the continuum of FFQ development for use in the Finnish adult population (Pietinen et al. 1988, Männistö et al. 1996, Paalanen et al. 2006). The strength of the validation study (II) was its large sample size (n=510), relative to other FFQ validation studies. As a limitation, the reference method, two 3-day FRs, included a limited number of reference days, compared with most of the earlier Finnish studies (Pietinen et al. 1988, Männistö et al. 1996), the classical FFQ validation study of the Nurses' Health Study (Willett et al. 1985), and many European studies (Goldbohm et al. 1994, Friis et al. 1997, McKeown et al. 2001) that have used FRs as the reference method. A sufficient number of recording days spread over the period covered by the FFQ is needed to capture within-person and potential seasonal variation in food and nutrient intakes, and thereby, to approximate true between-subject variation (Willett and Lenart 2013). Our FFQ validation study design did not meet entirely these requirements. Therefore, our findings might understate the validity of our FFQ.

A strength of Study III was our intent to estimate added sugar intake for the first time in Finnish adults, in contrast to using sucrose as a proxy measure for added

sugar intake. In light of the literature, studies using sugars per se as the exposure measure are scarce as the most common sugar exposure measure has been SSBs (Te Morenga et al. 2013, Louie and Tapsell 2015). Contemporary associations between added sugars and other dietary components contribute to the understanding of the diet complexity, and suggest that added sugars may act as a marker of other dietary components. It may therefore provide ideas for potential confounding factors and effect modifiers for future studies of added sugar and health outcomes. The main limitation of Study III was related to our explorative approach to study the association between added sugar intake and the remaining diet one-dimensionally, i.e. one macronutrient or food group at a time. A whole-diet approach, such as a healthy eating index (Kanerva et al. 2013, Kanerva et al. 2014) would have provided a complementary all-round view of the putative association between added sugar and unhealthy dietary habits in the general adult population.

Further strengths of this thesis include the size of the pooled sample in the analysis of the associations between dietary carbohydrate factors and obesity (IV), which was large in the context of Finnish studies. To our knowledge, there are no earlier Finnish studies that have investigated multiple carbohydrate measures in relation to obesity outcomes in a large population-based sample. Furthermore, we were able to study two different obesity measures, BMI and WC, which were based on measured estimates, thereby improving their accuracy. The main limitation of Study IV was its cross-sectional design. Cross-sectional studies provide information at one time-point and cannot establish temporal relations. It is very likely that reverse causation is one explanation for our findings, implying that obese individuals have diminished their carbohydrate and sugar intake. Some of this reverse causation may also be due to selective conscious and unconscious under-reporting of carbohydrate or sugar-containing foods (Johansson et al. 1998).

6.2 CARBOHYDRATE FACTORS AND THE FCDB (I, III)

The quality of the FCDB in terms of the studied nutritional factors is a fundamental element for nutritional epidemiological research (Slimani et al. 2007b). Together with study population, study design, dietary assessment method, and subject-related factors, carbohydrate factor values of the FCDB contribute to the individual carbohydrate factor levels of the study subjects. Value documentation represents one means through which the content and quality of FCDB can be managed and made more transparent (Becker et al. 2008).

GI values (I)

Apparently, no other study has examined whether existing controlled vocabularies, like the one described in EuroFIR, are suitable for GI values. In contrast to conventional FCDB components (i.e. nutrients) ideally assessed by chemical analysis of food, GI is a measure of the relative postprandial physiological response to food intake (Jenkins et al. 1981). In other words, the inherent nature of FCDBs relies on a reductionist approach to food because it purely seeks to describe the

chemical food composition without consideration of e.g. bioavailability. In contrast, GI describes how a carbohydrate-containing food is digested and metabolized in the body.

Despite these different starting points, we found that central dimensions of GI values, the origin and derivation method, could be documented with established controlled vocabularies of EuroFIR. This should be regarded as an initial step for improving the transparent incorporation of GI values into larger FCDB frameworks. We found also that storing the GI values in the Finnish national FCDB enabled direct profiting from FCDB standard recipes and the associated recipe calculation procedures. For example, the calculation of composite food GI and dietary GI and GL was facilitated due to the common calculation framework with the other carbohydrate values.

The assignment of GI values for a large number of foods has proved to be a challenging task (van Bakel et al. 2009b). This is foremost due to the lack of analysed values for local foods in many countries. Our GI database compilation process was comparable to those described in the literature (see Section 2.2.2, Table 2). Our GI database placed itself in the lower range in the contribution of zero values. The range of exact food matches varied considerably across studies (6-45%). In 67% of the studies providing information on exact food matches the contribution was higher than in our study (Flood et al. 2006, Olendzki et al. 2006, Schakel et al. 2008, Aston et al. 2010, Louie et al. 2011, Lin et al. 2012, Shyam et al. 2012, Sluik et al. 2016c). The highest contribution of exact matches was achieved in American studies (Flood et al. 2006, Olendzki et al. 2006, Lin et al. 2012), likely reflecting both superior research resources and better coverage of analysed GI values for the local foods. A GI value of a similar or closely related food was available for 29% of foods on our food list, whereas the range in the literature was 20-48%.

According to the literature, the calculation of GI values based on recipes was not a common way to derive GI values. In our study, along with the Finnish ATBC Study (Similä et al. 2009), and one American study (Schakel et al. 2008) the highest contributions of recipe calculation for GI value derivation were evident, 40%, 37%, and 38%, of all foods, respectively. This relates to the issue of whether the GI database operates in a common FCDB framework that includes standard recipes for multi-ingredient foods. The developers of the GI concept have suggested that GI is measured for single foods and calculated for mixed meals (Wolever and Jenkins 1986). This view has also received criticism due to analyses showing that the GI of mixed meals has a stronger correlation with fat and protein content of the meal than with carbohydrate content alone (Flint et al. 2004). Analyses of 102 American multi-ingredient foods revealed that 71% of foods were similarly categorized as low, medium, or high GI foods by calculating the values as compared with measuring them (Schakel et al. 2008). On the other hand, differences between calculated and measured GI values were seen for some sweetened dairy products and unsweetened breakfast cereals (Schakel et al. 2008). Reasons for such discrepancy include the fact that milk products, despite added sugars, induce rapid and high insulin response, which lowers blood glucose response and results in lower measured GI (Nilsson et al. 2004). In processed cereal products, fully hydrated starch may augment its rapid

hydrolysis to glucose resulting in high measured GI values (Brand et al. 1985). This confirms, that determination of food GI cannot solely rely on recipe calculation, which ignores the important effect of food processing on food GI value.

The EuroFIR controlled vocabularies need further elaboration to better serve full documentation of GI values. For instance, the documentation of the methodological criteria, as described in the ISO standard (International Organization for Standardization 2010), associated with the given GI value should be documented and made more transparent in databases. A large amount of food GI analyses has been conducted prior to the launch of the ISO standard, suggesting that the quality of GI analyses may have varied. The selection of GI values of sufficient quality from sources like the International Table of GI values (Foster-Powell et al. 2002, Atkinson et al. 2008) continue to rely on subjective decisions of the dataset compilers. The variation of GI values within a food category in the international table has been shown to be substantially larger than that arising solely from random error (Wolever 2013). It is therefore assumed that there are both true differences in GI values for foods within one category and methodological differences in GI measurement. In epidemiological settings, it is important that those foods contributing most to the interindividual variation in carbohydrate intake receive as reliable GI values as possible.

Given the overall large variation in the contribution of the different steps in GI assignment across studies and the true variation in the underlying diet of the study populations, a direct comparison of GI databases across the literature is challenging. On the other hand, the utilization of GI values with varying confidence level is probably one underlying reason for discrepant findings on the GI-health relationships in the literature.

Comparison of GI with other carbohydrate factors in FCDB (I)

The FFQ described in this thesis was based on 390 distinct food items linked to the Finnish national FCDB. Of these items, 209 were composite foods (mainly dishes), for which most carbohydrate factor values were derived through recipe calculation. The GI was an exception, as both analysed and imputed values were used in the GI value derivation method for composite foods. In this FCDB dimension, GI differs from the other carbohydrate factors. In contrast, regarding the basic ingredients (n=181), we found that there were no large differences in the derivation methods across the studied carbohydrate factors, including GI. In general, recipe calculation represents an effective way to arrive at nutrient values of composite foods (Reinivuo et al. 2009). Moreover, in FCDB update and management, chemical analysis of foods is directed towards analysis of the basic ingredients since it is more cost-beneficial and of a more universal nature compared to analysis of composite foods or dishes.

Added sugar intake estimation (III)

The estimation of added sugar is a relatively new phenomenon with varying methodologies. Inevitably, a common methodology would produce comparable results in epidemiological studies (Azais-Braesco et al. 2017). Moreover, a

standardized estimation method would improve nutritional surveillance, as upper limit values for added/free sugar are part of recent recommendations (Nordic Council of Ministers 2014, WHO 2015, Scientific Advisory Committee on Nutrition 2015). This is a challenge for FCDB updating and management.

A recent Dutch study based its added sugar estimation on thorough inspection of food groups based on FCDB information, food labels, and branded product information (Sluik et al. 2016b). Similarly, Louie et al. designed a 10-step decision algorithm for added sugar estimation on food by food basis in an Australian FCDB (Louie et al. 2015a).

Our added sugar estimation method was different from the other described methods as it relied entirely on standard recipes and food groupings of the Finnish national FCDB. This might have introduced some impurity to our added sugar estimate. For example, canned fruits and vegetables with added sugar were classified to the fruit and vegetable groups and contributed therefore to the estimate of naturally occurring sugar. However, this was true only for a small proportion of FFQ food items (14 out of 390 foods), and its effect on subject misclassification is considered small. In addition, our added sugar intake estimation was limited to sucrose and fructose. These sugars covered on average 76% of all mono- and disaccharides (excluding lactose) in women. In men, the corresponding proportion was 73%. Therefore, the estimated naturally occurring and added sugar intakes remain approximations of the true intakes. In a study investigating the carbohydrate content of Swedish market baskets, glucose contributed to total sugars with a similar amount as fructose (Becker et al. 2015). It is uncertain how the inclusion of the other saccharides (e.g. glucose) may have affected our results. However, our study did provide an approach to added sugar intake estimation (i.e. utilization of food grouping and standard recipes). It also represents an improvement to added sugar intake estimation relative to the situation where only sucrose intake is used as the proxy measure for added sugars. Overall, improvement of added sugar intake estimation methodology in future studies is warranted.

6.3 FFQ VALIDITY (II)

Our study protocol did not provide the possibility to assess the reproducibility of our FFQ in the DILGOM Study subjects. In earlier Finnish studies investigating FFQ performance, the intraclass correlation coefficients used to assess the consistency of the FFQ measurements on three or two separate occasions, respectively, have reached the level of 0.70 for carbohydrate factors (Pietinen et al. 1988, Männistö et al. 1996). In these studies, the time interval between the administrations was three months. According to the literature on FFQ reproducibility, correlation coefficients in the order of 0.50 to 0.70 are typical (Willett and Lenart 2013). This suggests that the reproducibility of carbohydrate intake measures has been acceptable in the forerunners of the current FFQ.

Cross-classification of subjects

Regarding the spectrum of carbohydrate factors considered in this thesis, only a few large studies in general populations have investigated the validity of whole-diet

FFQs in measuring carbohydrate factors beyond total carbohydrate and fibre. Of importance for epidemiological research is the ability of the FFQ to correctly rank subjects according to intake (Willett and Lenart 2013). We found that for all studied carbohydrate factors (except total sugars), around 70% of adult women were correctly classified into the same or the adjacent distribution quintile based on FFQs and two 3-day FRs. Similar figures were seen in men, although correct classification was slightly lower for starch (67%), total sugars (62%), and GI (65%).

Out of the 19 studies reviewed in this thesis, eight (Willett et al. 1985, Pietinen et al. 1988, Tjønneland et al. 1991, Männistö et al. 1996, Friis et al. 1997, Kroke et al. 1999, Toft et al. 2008, Sluik et al. 2016a) reported cross-classification results for several carbohydrate factors based on intake distribution quintiles of FFQ and the reference method. Correct classification into the same or the adjacent quintile ranged between 69% (Männistö et al. 1996) and 79% (Pietinen et al. 1988), the average being 73% in the eight studies. In addition, four studies reported ranking around 40% of the subjects into the same quartile (Bingham et al. 1997, Andersen et al. 1999, Brunner et al. 2001, McKeown et al. 2001). The comparison with other studies suggests that the ability of our FFQ in ranking subjects according to carbohydrate intake is comparable to the performance of FFQs used in epidemiological studies of other Western adult populations.

Correlation coefficients

In FFQ validation studies, correlation coefficients represent the most widely used statistical procedure to assess validity (Cade et al. 2004, Serra-Majem et al. 2009). Correlation captures the strength of the relationship between intake estimates based on the FFQ and the chosen reference method. Despite their wide use, correlation coefficients do not reveal systematic errors of dietary self-report, such as systematic misreporting of specific foods regardless of dietary assessment method or systematic errors of the shared FCDB (Willett and Lenart 2013).

In the present study, Spearman correlation coefficients between the FFQ and the two 3-day FRs for total carbohydrate (0.54 in women and 0.51 in men), starch (0.48 and 0.41), sucrose (0.46 and 0.49), and dietary fibre (0.58 and 0.67) compared well with those obtained from earlier Finnish studies, despite differences in study populations and validation study designs. The FFQ validation study of the ATBC study with male smokers (Pietinen et al. 1988) and the Kuopio Breast Cancer Study in postmenopausal women (Männistö et al. 1996) had extensive reference methods of twelve 2-day FRs within 6 months and two 7-day FR, respectively. Based on the literature reviewed in this thesis (Table 3), correlation coefficients in FFQ validation studies from other countries have showed correlations in the range of 0.40-0.70 for total carbohydrate and sucrose and 0.40-0.92 for dietary fibre. Although seldom reported, correlation results for polysaccharides are generally comparable to those of dietary fibre both in our study, and in the other studies (Goldbohm et al. 1994, Männistö et al. 1996, Bingham et al. 1997, Kroke et al. 1999, McKeown et al. 2001, Sluik et al. 2016a). Comparable to our result in both sexes, lactose intake has received high correlations, above 0.70, in both American and Finnish women (Willett et al. 1985, Männistö et al. 1996). This might be related to the regular

consumption pattern of most milk products, which facilitates their reporting and is sufficiently reflected in the food records.

The highest correlations for intakes of fibre and polysaccharides (0.74-0.92) were reported in two Dutch studies (Goldbohm et al. 1994, Sluik et al. 2016a). In the latter study, attention was paid to FFQ development and obtaining representative reference data with up to five (average 2.7) non-consecutive telephone-administered 24-hour DRs (Sluik et al. 2016a). Most importantly, subjects of that study included highly educated and motivated subjects already familiar with dietary reporting, which might exaggerate validity relative to studies conducted among the general population.

In the 10 studies reporting validation results for total sugars, the correlation coefficients have exceeded 0.45, which is higher than in our study (0.37 in women and 0.27 in men) (Goldbohm et al. 1994, Bingham et al. 1997, Riboli et al. 1997, Andersen et al. 1999, Kroke et al. 1999, Brunner et al. 2001, McKeown et al. 2001, Marks et al. 2006, Talegawkar et al. 2015, Sluik et al. 2016a). Similarly, our correlation coefficients for dietary GI and GL were also slightly lower than in the other five studies, showing correlation ranges between 0.53-0.69 and 0.32-0.70, respectively (Levitan et al. 2007, Barclay et al. 2008, Murakami et al. 2008, Du et al. 2009b, Barrett and Gibson 2010). The level of 0.40 was exceeded in our between-method correlations for GI in women, and GL in both sexes, but the correlation for dietary GI in men was low (0.31).

In general, the representativeness of the reference method is dependent on the day-to-day variation associated with the given dietary factor (Willett and Lenart 2013). A general explanation for our lower correlation coefficients may be the contribution of different food groups to carbohydrate intake, which were slightly different in the FFQ than in the two 3-day FR reference (see Appendix 3). Regarding GI, medium and high GI foods (cereals, and sugars, syrups, sweets and chocolate) were important carbohydrate sources in FRs. Foods with generally low GI (milk products, fruits, and vegetables) seemed to be emphasized in the FFQ. Compared with our study, the reference methods in many of the other studies have been more extensive (see Table 3). This might have improved the correlations, as all carbohydrate sources are likely to be sufficiently reflected.

Agreement between FFQ and two 3-day FRs

Nutritional epidemiology frequently utilizes relative (i.e. energy-adjusted) intakes rather than absolute intakes when assessing diet-health relationships. This concept was originally supported by the observation that energy-adjustment reduced some of the errors associated with self-report of absolute intakes (Willett and Stampfer 1986). We compared energy-adjusted intakes obtained by the FFQ and FRs. Overall, our FFQ consistently overestimated relative intakes of carbohydrate fractions and dietary GL compared with the FRs. The level of overestimation was mostly between 24% and 43%. A comparable overestimation pattern was evident for absolute estimates of carbohydrate factors in our study. Also in earlier FFQ validation studies that have used FRs as the reference method, an overestimation of intakes of some or all carbohydrate factors has been observed, although the magnitude of the overestimation has varied (Tjønneland et al. 1991, Riboli et al. 1997, Bingham et al.

1997, Brunner et al. 2001, McKeown et al. 2001, Marks et al. 2006, Paalanen et al. 2006, Sam et al. 2014).

We examined the agreement of our FFQ and the reference method across the range of intakes by using the Bland-Altman method and extended this analysis to age, education, and BMI – subject characteristics that might affect dietary reporting (II). We found that with increasing relative intake levels and increasing age there was bias mostly towards overestimation by the FFQ compared with FRs, more frequently in women than in men. A shift from the highest educational group to a lower educational group was associated with bias towards underestimation with the FFQ compared with FRs. We did not observe an association between BMI and between-method agreement in any of the studied carbohydrate factors. This suggests that at the population level, subjects across the BMI range are consistent in their reporting with the two methods.

Thus far, the evaluation of subject characteristics in relation to FFQ validity has been formally incorporated in only a few FFQ validation studies that have used another dietary method as a reference. In an Australian validation study including 96 adults aged 25-74 years, age was not associated with dietary reporting (Marks et al. 2006). Another Finnish study reported that correlation coefficients between FFQ and 3-day FR did not vary by age in men, but correlation coefficients were generally lower in 30- to 50-year-old women than in older women (Paalanen et al. 2006). High BMI has been associated with lower FFQ performance in estimation of carbohydrate, fibre, and total sugar intake, assessed with both correlation coefficients (Paalanen et al. 2006) and between-method agreement (Marks et al. 2006).

Overall, there are several potential reasons why subject characteristics might affect dietary reporting. In modern society, overestimation of foods perceived as socially desirable and underestimation of foods perceived as undesirable are likely to occur (Johansson et al. 2001). Ageing may impair dietary reporting, as the FFQ represents a demanding cognitive task and relies on both conceptualizing of the questions and memory (McNeill et al. 2009). It might be assumed that along with ageing and weight gain, the pressure to eat healthy increases as individuals notice health challenges.

Energy under-reporting represents one of the best-established challenges for all dietary self-report methods. A systematic review based on 37 studies found that the median prevalence of energy under-reporting in FRs has been around 30%. The review suggested that female sex, old age, lower education, and BMI were frequently associated with energy under-reporting (Poslusna et al. 2009). A pooled analysis of five FFQ validation studies with doubly labelled water as an objective measure of energy intake confirmed that age, education, and high BMI were predictors of energy under-reporting also in FFQs (Freedman et al. 2014). Our study confirmed that in the Finnish adult population energy under-reporting was more common in the obese than in the non-obese (IV). This might suggest that energy under-reporting is also due to under-reporting of carbohydrate foods because of their high contribution to energy intake in Western countries, including Finland (Paturi et al. 2008, Helldán et al. 2013). For example, there are data to show that energy under-reporters avoid foods rich in sugar (Johansson et al. 1998). In our study, energy

under-reporting was less common among subjects with high added sugar intake (III). Some of these effects could underlie our findings of the effect of subject characteristics on the between-method agreement in measuring dietary carbohydrate factors. In all, our FFQ validation results (II) form the basis for interpretation of findings in Studies III and IV of this thesis. They also shaped our analytical choices. For example, age and education were included as central confounders, and energy under-reporting was taken into account in the analyses of Studies III and IV.

6.4 ADDED SUGAR AND OTHER DIETARY COMPONENTS (III)

Sociodemographic determinants of added sugar intake

In our study, subjects with high added sugar intake were likely to be younger than subjects with low intakes (III). Similar findings have been observed in other population-based studies (Bowman 1999, Parnell et al. 2008, Sluik et al. 2016b). In contrast, those in the highest quartile of naturally occurring sugar intake (from fruits and vegetables) were more likely to be older, suggesting that fruits and vegetables are more pronounced as sugar sources in the older age groups of the Finnish adult population. These findings together suggest that the modern food environment may have especially shaped the diets of the younger generations. Reducing added sugar intake and counteracting any increase in intake especially among the young would therefore be important for public health.

We did not observe any statistically significant trends in the proportion of low educated subjects or physically inactive subjects when shifting from the lowest added sugar intake quartile to the highest quartile (III). In-depth analysis of these phenomena in the Finnish adult population remains outside the scope of this thesis. According to the literature, the sociodemographic determinants of added sugar intake are generally poorly documented and require further investigation (Azais-Braesco et al. 2017). Thus far, trends between added sugar intake and lower socioeconomic status have been reported in mainly American studies, in which SSBs represent a major, easily affordable source of added sugar (Bowman 1999, Han and Powell 2013, Drewnowski and Rehm 2014). Generally, identification of adult population groups with high added sugar intake is seen as important for designing of programmes and policies to restrict added sugar intake (Park et al. 2016).

Fat intake and fat-providing foods

Similar to earlier studies mainly conducted in the 1990s (Baghurst et al. 1992, Baghurst et al. 1994, Lewis et al. 1992, Emmett and Heaton 1995, Bolton-Smith and Woodward 1994, Gibson 1996, Flynn et al. 1996), we found an inverse association between energy-adjusted added sugar (expressed as E% in the earlier studies) and fat intake (III). This suggests the existence of a sugar-fat seesaw phenomenon (Sadler et al. 2015) in the Finnish adult population. In terms of dietary fat quality, it is relevant to ask, whether a relative increase in added sugar intake has an impact on intake of different fatty acids or foods that are important sources of these fatty acids. Such

associations may be of importance since current nutrition recommendations emphasize fat quality over fat quantity (Nordic Council of Ministers 2014).

In the Dietary and Nutritional Survey of British adults in 1986-1987, inverse relationships were reported between intake of added sugar and saturated, monounsaturated, and polyunsaturated fatty acids (Gibson 1996). Intake of total sugars, and sucrose as E% have also been found to be inversely associated with intake of different fatty acids in other British, German, and Australian populations (Gibney et al. 1995, Linseisen et al. 1998, Cobiac et al. 2003). A Dutch study observed that adults adherent to added sugar recommendations tended to have higher saturated fatty acid intakes (Sluik et al. 2016b). This suggests that dietary fat quality may be compromised in subjects with low added sugar intakes, as added sugar energy is replaced by energy from saturated fat. Unfortunately, our study did not include an analysis of the association between added sugar and fatty acids, but rather took the approach of evaluating fat intake at the food group level.

We found around 30% higher intakes of butter and butter mixtures in the highest added sugar intake quartile than in the lowest quartile (III). In our study, further suggestive evidence of compromised fat quality in subjects with high added sugar intakes was the finding that intakes of vegetable margarine and fish were approximately 20% and 27% lower in the highest added sugar intake quartile than in the lowest quartile. The results on lower fish consumption in subjects with high added sugar intake are in line with results from the USDA Continuing Survey of Food Intakes by Individuals in 1994-1996 including a nationally representative sample of 14 709 individuals (Bowman 1999). Dutch adults adhering to the <10 E% added sugar recommendation were also found to score higher on the fish component of the Dutch Healthy Diet Index (Sluik et al. 2016b). In all, the relation between added sugar intake and dietary fat quality seems mixed, thus warranting further investigation. It should especially be confirmed whether studies at the food group level and the nutrient level produce congruent results.

Fibre intake and fibre-providing foods

Good carbohydrate quality, including high intake of whole-grain cereals, vegetables, and fruits, and low intake of foods with high added sugar content, is a key element of food-based dietary guidelines (National Nutrition Council 2014). This is reflected in the nutrition recommendations of total carbohydrate and fibre (National Nutrition Council 2014, Nordic Council of Ministers 2014). We found an inverse association between energy-adjusted added sugar and fibre intake independent of age, leisure-time physical activity, smoking status, education, and BMI (III). Comparable results have emerged in large population-based studies in other countries (Bolton-Smith and Woodward 1995, Cobiac et al. 2003, Marriott et al. 2010).

High added sugar intake has been associated with lower intakes of fruits, vegetables, and grains in several representative population-based studies (Bowman 1999, Britten et al. 2000, Cobiac et al. 2003), as well as in smaller studies with less than 2000 subjects (Baghurst et al. 1992, Lewis et al. 1992, Drewnowski et al. 1997). Among recent studies, Sluik et al. found that adults adhering to the <10 E% guideline for added sugar, scored higher on the Dutch Healthy Diet Index

components of fruits and vegetables (Sluik et al. 2016b). Our study confirms these earlier findings. In women, the relative decrease in fruits, vegetable, and rye intakes was around 30% when shifting from the lowest to the highest added sugar intake quartile. In men, the decrease was slightly smaller, yet statistically significant: 11%, 24%, and 21% for these food groups, respectively. Overall, studies are consistent in suggesting that with increasing added sugar intake, fibre intake and related healthy food choices (intakes of fruits, vegetables, high-fibre cereal products) may be compromised.

6.5 OBESITY (III, IV)

Total carbohydrate, dietary GI, and dietary GL

According to nutrition recommendations, carbohydrates should provide the largest share to dietary energy, as central carbohydrate sources, such as fibre-rich cereal products, and fruits have a high nutrient density and a low energy density (Nordic Council of Ministers 2014). High GI diets have been hypothesized to promote excessive weight gain due to their postprandial effect in inducing a rapid rise in blood glucose levels, following reactive hypoglycaemia, thereby disturbing food intake regulation (Ludwig 2002). This mechanism may apply to high GL diets.

In our meta-analysis of three cross-sectional population-based studies with 12 342 adult subjects, total carbohydrate intake and dietary GL were inversely associated with both general obesity defined as $\text{BMI} \geq 30 \text{ kg/m}^2$ and abdominal obesity defined as elevated WC $\geq 88 \text{ cm}$ in women and WC $\geq 102 \text{ cm}$ in men (IV). Similar findings for total carbohydrate intake have been observed in both cross-sectional (Bolton-Smith and Woodward 1994, Merchant et al. 2009) and some prospective cohort studies (Colditz et al. 1990, Ludwig et al. 1999). However, the majority of prospective cohort studies have failed to show associations between total carbohydrate intake (Haffner et al. 1991, Parker et al. 1997, Ma et al. 2005, Iqbal et al. 2006) or GL (Ma et al. 2005, Hare-Bruun et al. 2006, Du et al. 2009a) and obesity measures. It has been recognized that in European populations dietary GL most probably acts as a marker of carbohydrate intake, and average GL varies considerably across countries (van Bakel et al. 2009a). Due to the definition and calculation method of dietary GL, two comparable diet GL values may originate from very different food intake patterns (variation in GI, amount of carbohydrate, or both). Against this background, it is not surprising that the associations between carbohydrate intake or dietary GL and obesity outcomes have been inconsistent. However, the food source of carbohydrates has been shown to affect its relation to obesity, as carbohydrates from fruits and vegetables have been associated with lower WC in a 5-year follow-up of European adults (Halkjaer et al. 2006).

Despite an overall null result for the GI-obesity relationship in our study, we observed an inverse association between dietary GI and obesity in men. Furthermore, the inverse association between GL and obesity appeared stronger in men than in women (IV). Dietary sources of carbohydrates in Finnish men and women are slightly different from each other. Beverages (e.g. beer), potatoes, and rye bread mainly made from milled flour (all generally high GI) contribute as ingredient

groups more to the carbohydrate intake in men, whereas fruits and berries and milk products (generally low GI) are emphasized in women (Paturi et al. 2008, Helldán et al. 2013). Despite a very similar mean GI in women and men observed in our study (II, IV), the contributing dietary patterns may vary.

The different carbohydrate sources across populations together with challenges of GI databases compiled for epidemiological study purposes might explain why dietary GI is not consistently associated with obesity (Ma et al. 2005, Hare-Bruun et al. 2006, Du et al. 2009a, de la Fuente-Arrillaga et al. 2014). Moreover, the chosen obesity measure might be of importance for observing a significant association. In two studies based on large samples of European adults, dietary GI was positively associated with WC change and change in visceral adiposity, but not with general adiposity based on BMI (Du et al. 2009a, Romaguera et al. 2010). Average intake estimates for carbohydrates, and average GI and GL seemed higher in our study than in other European countries as measured with FFQs (Du et al. 2009a, Romaguera et al. 2010) or 24-hour DRs (Cust et al. 2009, van Bakel et al. 2009a). Combined effects of local eating habits (e.g. high consumption of cereal products) and high GI values assigned for locally important foods (e.g. rye bread) may contribute to higher GI and GL in Finns. Taken together, it seems that dietary GI or GL or even dietary carbohydrate content alone is not a useful predictor of obesogenic diets. Therefore, the meaning of these carbohydrate factors should be interpreted in the total dietary context, which may differ from population to population.

Dietary fibre

Fibre intake of Finnish adults has slightly decreased during the last decades, partly due to a decrease in intake of rye bread (Raulio et al. 2013). However, fibre intake seems to be higher in Finland than in other European countries (Cust et al. 2009, Raulio et al. 2013). Although we did not observe any association between fibre intake and overall obesity, fibre intake was associated inversely with abdominal obesity (IV). Large prospective cohort studies in USA (NHS and HPFS) and Europe (EPIC) have shown findings in a similar direction (Koh-Banerjee et al. 2003, Liu et al. 2003, Du et al. 2010). Findings of the EPIC study have suggested that especially cereal fibre would be beneficial for counteracting both overall obesity and abdominal obesity (Du et al. 2010).

Added sugars and sucrose

Added sugars are considered detrimental to health primarily because of their nutrient density-diluting effect. Added sugars, especially in the form of SSB, are suggested to increase obesity risk mainly due to their energy-providing nature (Te Morenga et al. 2013). Whether added sugars or sucrose (the main sweetening agent used in households and in the food industry) per se are associated with obesity has seldom been assessed in population-based studies. Our study (IV) tested the hypothesis, of higher relative intake of total sucrose being associated with the likelihood of having been obese at one time-point.

Our findings that added sugars (sucrose and fructose) (III) and total sucrose (IV) were inversely associated with obesity are not unique, as earlier cross-sectional

studies have produced similar results using total carbohydrates, total sugars, extrinsic sugars, or sucrose as carbohydrate intake measures (Bolton-Smith and Woodward 1994, Drewnowski et al. 1997). More recently, an analysis in 1742 adults participating in the EPIC Norfolk Study in the UK showed an age- and sex-adjusted OR of 0.56 (95% CI 0.40-0.77; highest vs. lowest quintile) for the sucrose-overweight/obesity relationship in a 3-year follow-up (Kuhnle et al. 2015). The dietary assessment of that study relied on 7-day FRs. Thus far, the intakes of individual sugars or added sugars in relation to obesity outcome have been investigated in very few prospective studies, and no significant associations have been detected (Colditz et al. 1990, Haffner et al. 1991, Parker et al. 1997). Shortcomings of FCDBs might explain the lack of studies.

Methodological considerations related to dietary carbohydrates and obesity

There are several explanations that might contribute to an inverse or null association between total sucrose and obesity measures. First, sucrose originates from foods and dishes that are sweetened with sucrose, but also fruits and vegetables are an important source of sucrose (Paturi et al. 2008, Helldán et al. 2013). In our study, the inverse sucrose-obesity relationship appeared stronger in subjects with high fruit intake than in those with low fruit intake (IV), suggesting that fruit intake has the potential to modify the apparent association between sucrose intake and obesity. Second, both sucrose and added sugar intake estimates may be inaccurate due to shortcomings of dietary self-report methods. We found acceptable relative validity of our FFQ in measuring sucrose intake, but slightly poorer relative validity for fructose (II). Studies with the sugar intake biomarker have suggested that serious under-reporting of sugar intake may occur with obese subjects (Kuhnle et al. 2015). This kind of selective misreporting could not be demonstrated in our study due to lack of biomarker data. However, the exclusion of energy under-reporters, as defined by the Goldberg cut-off values (Goldberg et al. 1991) did not change the result of Study IV. It is very likely that this procedure does not fully eliminate the bias of dietary misreporting.

Finally, a central limitation of our study (III, IV) and other studies in the field of dietary carbohydrates (e.g. added sugars) and obesity outcomes is related to the possibility of reverse causation. In practice, obese individuals may have changed their diet (i.e. decreased their intake of carbohydrate- and sugar-containing foods) as a consequence of overweight, obesity, and possible comorbidities. Overall, reverse causation is especially relevant for cross-sectional studies, but also affects cohort studies. A recent comparison of different modelling approaches for evaluating diet, physical activity, and long-term weight gain in NHS and HPFS cohorts found that investigating changes in diet and physical activity is superior to other approaches in determining the effects on concurrent long-term weight gain (Smith et al. 2015). In other words, in longitudinal studies of free-living populations, repeated measures of diet and weight during follow-up may reduce reverse causation bias. In general, this may help to produce more consistent findings on the relationship between dietary carbohydrates and health outcomes, including obesity.

6.6 FUTURE PERSPECTIVES

Declining participation rates are likely to affect dietary intake estimates of future population-based studies, as low socioeconomic status – one of the determinants of non-participation – has been associated with unhealthy dietary habits and poorer health behaviour. Therefore special emphasis should be given to the recruitment process when nationally representative samples are pursued. This would benefit epidemiological research, since adequate ranges of studied dietary intakes are important for obtaining reliable results.

Readers of dietary epidemiological research papers should be provided with tools to more easily interpret the certainty of intake assessment from the FCDB perspective. Origin and derivation method of the dietary factor values do not capture all dimensions relevant for judging their confidence level. This has come to light as research interests have been directed towards dietary factors that are not standard components of FCDBs, current examples being GI and added sugars. In the Finnish national FCDB, recipe calculation procedures are central in obtaining any dietary factor value for dishes and multi-ingredient foods. Therefore, the accurateness of intake assessment (e.g. fibre, mono- and disaccharides, GI) from the view-point of FCDBs will continue to be dependent on understanding of the contemporary food recipes used in households, catering services, and the food industry.

Future studies on the relationship between added sugars and other dietary components and health outcomes would benefit from a standardized and validated estimation method of added sugars. A standardized methodology would also enable more accurate monitoring of added sugar intakes in the general population. The inclusion of added sugar values into FCDBs could be a common target of the organizations responsible for national FCDB contents in different countries, e.g. in Scandinavia and Europe, where the common principles of FCDB frameworks already exist. Efforts should be directed towards updating and managing FCDBs so that central product formulations and food recipes are reflected in FCDB content. This will require co-operation with the different stakeholders responsible for food legislation and labelling as well as the food industry.

Dietary intake assessment of this thesis relied on a FFQ designed for epidemiological studies in the Finnish adult population. Energy-adjustment was applied throughout the studies, which may alleviate some of the distorting effect of energy under-reporting on dietary intake estimates. Despite this, our results indicate that subject characteristics may introduce differential bias and misclassification to diet-health analyses. Therefore subject characteristics should further be incorporated into modelling of diet-health associations along with separate consideration of energy under-reporting. In general, biomarkers represent an opportunity to complement traditional dietary intake assessment methods and implement measurement error corrections. In the field of dietary carbohydrates, several promising biomarkers are under intensive investigation. Overall, sophisticated measurement error correction techniques are a necessity for future nutritional epidemiological studies. This, in turn, requires that dietary information will continue

to be gathered with multiple different dietary methods. Due to the changing food environment, the need for validation of dietary assessment methods is ongoing.

Diet is inherently complex. This was highlighted in our study by the multiple associations between added sugar and other dietary components. To generalize, this kind of phenomenon exists for all carbohydrate factors studied in this thesis. Results obtained for one dietary factor should be interpreted in the context of total diet overall. Studies utilizing the whole-diet approach, such as *a priori* and *a posteriori* dietary patterns or indices/scores, may prove useful in understanding the significance of single carbohydrate factors in the total dietary context.

Obesity represents a challenging outcome due to its multifaceted aetiology. Further prospective cohort studies are needed to elucidate the temporality and the strength of the associations between carbohydrate factors and adiposity. There is room for improvement in study designs and versatility of measurements, including metabolic factors, to be considered in the analyses. In addition to general improvements of dietary intake assessment, repeated measurements of both exposure and outcome during the follow-up period would be important. Studies should seek to identify subtle changes in diet that are relevant for the obesogenic process.

7 SUMMARY AND CONCLUSIONS

The aim of this thesis was to contribute to the current understanding of carbohydrate intake measurement methodology in the Finnish adult population. Associations between added sugar intake and other dietary components as well as associations between carbohydrate factors and obesity outcomes were also investigated. The main findings and conclusions of this thesis can be summarized as follows:

1. The origin of GI values and the methods used to derive them were acceptably documented with controlled vocabularies when adding them to the Finnish national FCDB. This procedure has the potential to aid comparison of GI information across FCDBs and add transparency. However, further development of the vocabularies is needed to fully suit documentation of GI values.
2. Compared with previous studies, the FFQ designed to measure the habitual diet of Finnish adults seemed to have an acceptable relative validity in assessment of carbohydrate factors (i.e. total carbohydrate, starch, total sugars, fructose, lactose, sucrose, dietary fibre, insoluble dietary fibre, soluble polysaccharides, dietary GI and GL). However, future study results concerning intake of total sugar and dietary GI in men should be interpreted cautiously. Overall, the FFQ can be used in carbohydrate intake assessment of epidemiological studies that seek to rank subjects according to carbohydrate intake.
3. Subject's age and, to a lesser extent, education were associated with diminished agreement between FFQs and FRs in measuring carbohydrate factors (see point 2 for definition of carbohydrate factors), especially in women. BMI was not associated with the between-method agreement. This supports the rationale for including age and education as confounders in epidemiological analyses.
4. Adults with high intake of added sugars were younger than those with low added sugar intake. Added sugar intake was associated with lower fibre intake, reflected in lower intakes of fruits, vegetables, and rye. Added sugar intake was also associated with lower intake of fish and higher intakes of butter and butter-mixtures. When investigating health effects of added sugar, confounding by other nutrients and foods should be considered. In addition, a standardized methodology of added sugar intake estimation and the inclusion of added sugar values into FCDBs are needed.
5. In cross-sectional studies of Finnish adults, intake of total carbohydrate, sucrose, and dietary GL were associated inversely with obesity. The inverse

association between total sucrose intake and obesity was stronger in subjects with high fruit intake, than in subjects with lower fruit intake. These findings suggest that obese individuals may be prone to lower their carbohydrate intake or selectively underreport intakes of carbohydrate-rich and sugar-containing foods. Further studies in carefully designed longitudinal settings are needed. In addition to sucrose, added sugars should be investigated.

ACKNOWLEDGEMENTS

This work was carried out at the National Institute for Health and Welfare (THL), previously the National Public Health Institute, in 2008-2018. I would like to thank the Institute, the department heads, and the unit heads for providing excellent research facilities. Special thanks go to Research Professor Markku Peltonen, long-standing head of the unit in THL, and Professor Johan Eriksson, who supported my work during the early years of my career. I am also grateful to the leaders, research personnel, and participants of the FINRISK and FINDIET 2007 Studies, the DILGOM Study, the Health 2000 Survey, and the HBCS for making research with such high level datasets possible.

I gratefully acknowledge the personal funding I have received to carry out this work: the Doctoral Programmes in Public Health (DPPH), which at the latest stage of my studies changed to the Doctoral Programme in Population Health within the Doctoral School of Health Sciences at the University of Helsinki, the Finnish Cultural Foundation, the Juho Vainio Foundation, the Yrjö Jahnsson Foundation, and the University of Helsinki.

My deepest gratitude goes to my supervisors Adjunct Professor Satu Männistö and Adjunct Professor Liisa Valsta. Your broad expertise has guided me throughout the years, helping me view nutritional science from different perspectives. Under your guidance, I have started penetrating the mysteries of nutrition monitoring in the Finnish adult population – I am more than grateful for this experience! Satu, your deep dedication to nutritional epidemiology and its methods has been one of the best sources of inspiration. I deeply respect your expertise and appreciate all the lessons learnt during the years we have worked together. Your generous support and enthusiasm have made this an interesting and rewarding journey. Liisa, your expertise and wide range of interests in the field of human nutrition are awe-inspiring. Your positive attitude and confidence in me and the future in general have been invaluable. I admire your enthusiastic mind.

Adjunct Professor Hanna Lagström and Professor Wulf Becker were the official reviewers of this thesis. I thank them both for their professional engagement in the thesis examination and their insightful comments. I am also grateful to Adjunct Professor Arja Erkkilä for accepting the role of opponent. I also thank Professor Ossi Rahkonen from the Department of Public Health, University of Helsinki, for serving as custos, and his kind guidance through the academic dissertation process.

I am grateful to all of my co-authors for their contribution, valuable criticism, and comments on the thesis articles. Your expertise in the fields of food composition databases, statistics, and nutrition was indispensable. Special thanks go to Professor Paul Knekt for sharing his knowledge of epidemiological analysis related to meta-analyses and nutritional epidemiology in general.

All of my former and present colleagues at THL, beyond unit boundaries, are highly appreciated. The encouraging atmosphere in the units has brought me joy over the years. I feel privileged to have shared my everyday work with so many

wonderful people including Heli Tapanainen, Heli Reinivuo, Heikki Pakkala, Katja Borodulin, Minna Similä, and Katja Hätönen, just to mention a few. Thank you all for sharing your thoughts and the many uplifting moments. Tuija Jääskeläinen, thank you, for sharing joys and sorrows concerning the thesis finalization process. Leonie-Helen Bogl, Katri Sääksjärvi, and Noora Kanerva, thank you for friendship and stimulating discussions on nutritional epidemiology and research in general. You mean a lot to me.

I am grateful to my friends for their unquestioning support and help in putting work into perspective. Jenni, Paula, and Annika, – there is a special place in my heart for everything I have experienced with you. You have all helped me to understand my personal targets and many interesting phenomena in life. Great friendships are meant to last lifelong.

I warmly thank my parents-in-law for all their support and caring. All the practical help and shared moments mean a great deal to me. Coping with the busy years of working full-time, studying, and raising children would not have been possible without you. My own parents, my brother and his family, and my sister deserve my deepest appreciation. You are an invaluable source of strength and delight in life. You remind me again and again that love conquers all.

Finally, my dear husband Ville and our beloved children Kaapo and Kiira-Kerttu, you are the brightest lights of my life. During these thesis years, your patience and unconditional love have been the greatest resources of all. You continue to lift me up.

Järvenpää, May 2018

Niina Kaartinen

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APPENDICES

Appendix 1.

Equations for calculation of composite food glycaemic index (GI) values (including an example), dietary GI, and dietary glycaemic load (GL).

$$GI = \frac{\sum_{k=1}^n \frac{p \times CHO_k \times GI_k}{\sum_{k=1}^n p \times CHO_k}}$$

Equation 1. Calculation of the GI value of a composite food, where k is the ingredient, CHO is the glycaemic carbohydrate/100 g, p is the proportion of the ingredient in the recipe, and n is the number of ingredients in the recipe (WHO 1998).

Example: Composite food GI value calculation for traditional fish soup.

	Carbo- hydrate g/100g ingredient	Proportional contribution of ingredients in food recipe	Carbo- hydrate g/100g ready food	Proportion of carbohydrate/ Carbohydrate in food	Ingredient GI	Proportion x GI
	CHO_k	p	$p \times CHO_k$	$\frac{p \times CHO_k}{\sum p \times CHO_k}$	GI_k	$\frac{p \times CHO_k \times GI_k}{\sum p \times CHO_k}$
Salt	0	0.001	0	0	0	0
Wheat flour	63.6	0.009	0.57	0.11	75	8.5
Potato	13.20	0.25	3.35	0.66	88	58.3
Onion	4.80	0.05	0.23	0.05	43	1.9
Milk	4.80	0.19	0.91	0.18	33	5.9
Coalfish	0	0.19	0	0	0	0
Water	0	0.47	0	0	0	0
Cooking fat	0	0.01	0	0	0	0
Sum			5.1	1		74.6

$$\text{Dietary GI} = \frac{\sum_{k=1}^n \frac{CHO_k \times GI_k}{CHO_{tot}}}$$

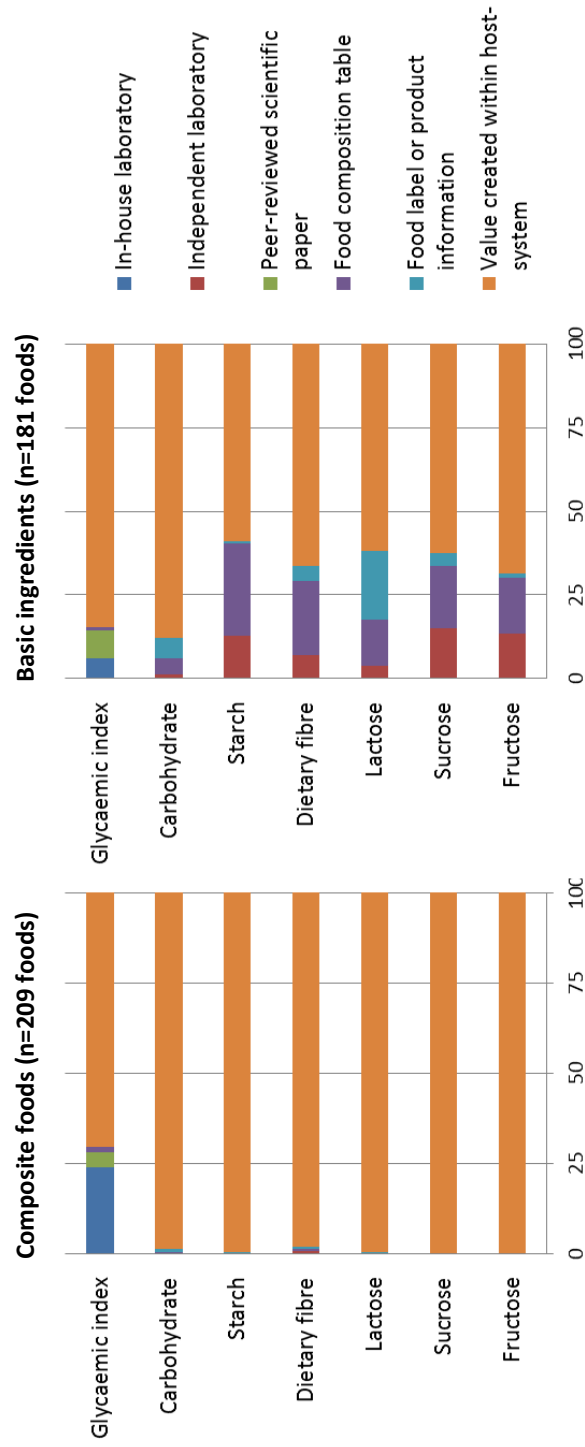
$$\text{Dietary GL} = \sum_{k=1}^n CHO_k \times \frac{GI_k}{100}$$

Equation 2. Calculation of the dietary GI and GL values, where k is the food, CHO_k is the glycaemic carbohydrate consumed from the k^{th} food (g), GI_k is the GI of the k^{th} food, and CHO_{tot} is the amount of glycaemic carbohydrates in the entire diet (Wolever et al. 1991, Wolever et al. 1994, Salmerón et al. 1997)

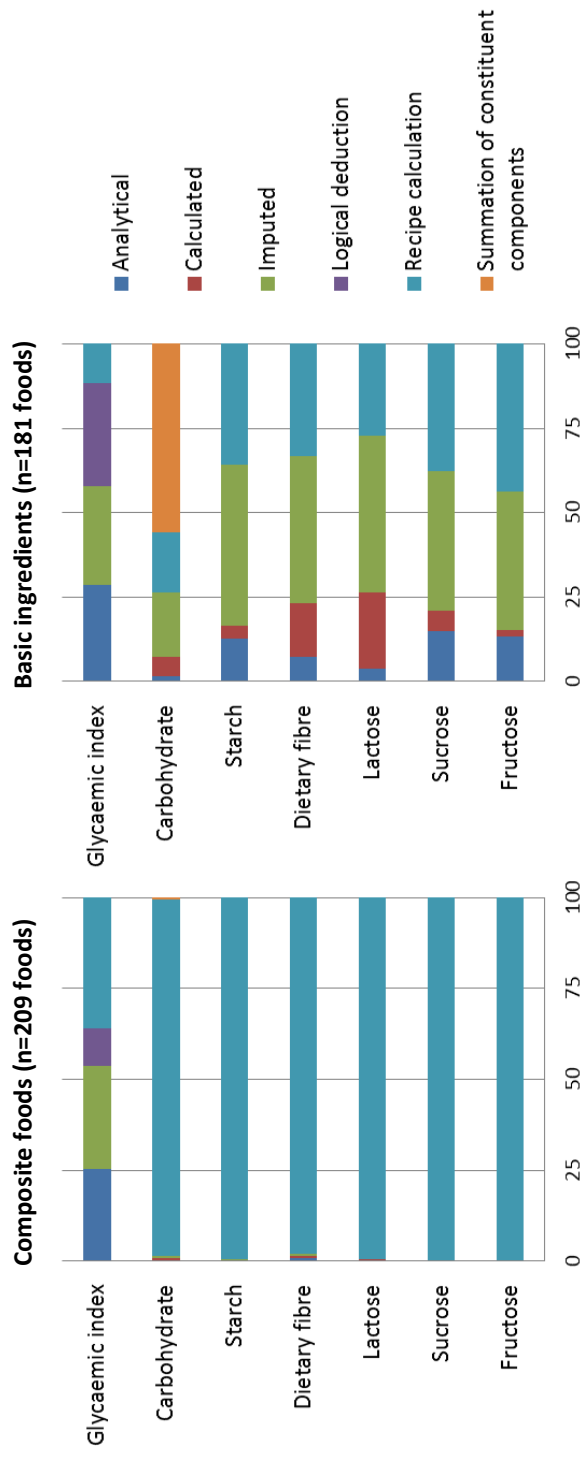
Appendix 2.

Contribution (%) of EuroFIR Acquisition type (A) and Method type (B) thesauri value descriptors of carbohydrate factors for foods encoded in the FFQ (n=390 after exclusion of duplicate foods) and the Finnish national food composition database.

A. Acquisition type (value origin)



B. Method type (method of value derivation)



Appendix 3.

Contribution (%) of ingredient food groups to intake of total carbohydrate, fructose, sucrose, and dietary fibre based on the food frequency questionnaire and two 3-day food records.

	<i>Women</i>		<i>Men</i>	
	FFQ	Two 3-day FR	FFQ	Two 3-day FR
	Contribution (%)			
Total carbohydrate				
Cereals	41	43	42	46
Milk and milk products	13	12	12	10
Fruits and berries	13	11	9	8
Sugars, syrups, sweets and chocolate	10	13	9	11
Potato and potato products	7	6	10	8
Soft drinks and juice	7	6	9	7
				91% *
Vegetables and legumes	6	5	4	3
Alcoholic beverages	1	1	3	4
Other food groups	3	3	3	3
Fructose				
Fruits and berries	48	48	38	45
Vegetables and legumes	19	18	15	15
Soft drinks and juice	19	16	31	21
Milk and milk products	7	6	4	3
				88% *
Sugars, syrups, sweets and chocolate	2	6	3	7
Other food groups	5	7	8	9
Sucrose				
Sugars, syrups, sweets and chocolate	39	45	40	44
Fruits and berries	18	17	14	15
Soft drinks and juice	17	17	24	24
Milk and milk products	15	12	10	10
				90% *
Vegetables and legumes	5	5	4	3
Other food groups	6	5	7	5
Dietary fibre				
Cereals	48	50	54	60
Fruits and berries	22	21	18	16
Vegetables and legumes	21	19	18	14
				90% *
Potato and potato products	4	4	6	5
Other food groups	4	6	4	4

* Average contribution of food groups indicated above the horizontal line

Appendix 4.

Spearman rank-correlation coefficients between crude daily intakes of food groups based on food frequency questionnaires and two 3-day food records.

	Women (n=292)	Men (n=218)
Food group (g/day)		
<i>Carbohydrate sources</i>		
Sugars and syrups	0.50	0.55
Sweets and chocolate	0.57	0.44
Soft drinks	0.35	0.46
Fruit and berry drinks	0.30	0.39
Fruits	0.42	0.62
Berries	0.56	0.66
Fruit juices (100%)	0.37	0.36
Vegetables ¹	0.35	0.40
Cereals ²	0.42	0.44
Rye	0.54	0.58
Wheat	0.41	0.48
Potatoes and potato products	0.34	0.42
Milk and milk products	0.68	0.69
Alcoholic beverages	0.75	0.68
<i>Other food groups</i>		
Meat and meat products	0.46	0.33
Fish, fish products and shellfish	0.40	0.35
Butter (including butter oil mixtures)	0.52	0.53
Vegetable margarine	0.53	0.56
Coffee and tea	0.56	0.56

¹ Excluding legumes and nuts.

² Includes rye, wheat, oat, barley, pasta rice, other cereals, and starches.